## Thyroxin Levels Associated with Current Suicide Attempts: A Case Control and Follow-Up Study

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#### **ABSTRACT:**

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**Objective:** Suicide is a complex behavior concerning a number of psychological, biological, social and cultural factors. It is also an important public issue, as well as one of the leading causes of death. We aimed to examine the relationship between suicide attempt and thyroid hormones in suicide attempters and healthy controls and aimed to clarify whether any of the thyroid hormone levels may have predicted current or future suicide attempts.

**Method:** This study comprised 358 participants (115 suicide attempters, 243 controls). Thyroid hormone levels including free T3, free T4, and TSH of all participants were explored. For predicting future suicide attempts using our hospital database and the database of the Republic of Turkey Social Security Institution, via International Classification of Diseases (ICD) diagnostic codes related to suicide data of future suicide attempts of the study participants were collected. Participants were people without previous history of any thyroid disorder or chronic disease (endocrinological, pulmonary, gastrointestinal, neurological, infectious and neoplastic diseases, hepatic, renal or cardiac failure) that may affect thyroid hormone levels. The participants who were on any thyroid hormone or drug that may affect thyroid hormone levels (e.g., lithium, carbamazepine, oral contraceptives etc.) alcoholism or drug abuse other than nicotine, pregnancy, detected possible thyroid disease during procedure, intellectual disability, rejection of blood tests, missing data on topics mentioned above, were all excluded.

**Results:** Thyroid hormone levels of both groups were within normal range. Groups differed with regard to FT4 (thyroxin), TSH and FT3/FT4 levels. A logistic regression model indicated that suicide attempters were 32.7 times more likely to have higher FT4 levels (OR: 32.7; 95% CI: 5.3-202.9; p<0.0001), 1.7 times more likely to have higher TSH levels (OR: 1.7; 95% CI: 1.2-2.3; p=0.002), 2.5 times more likely to have lower FT3/FT4 levels (OR: 0.4; 95% CI: 0.2-0.8; p=0.008) than controls. Diagnostic validity of FT4 was found to be good in differentiating patients with both groups (ROC area under the curve=0.821; 95% CI: 0.77-0.87; p<0.0001). The cut-off point for FT4 of 1.15 ng/dl gave a high sensitivity (85%) and specificity (70%).

**Conclusion:** Thyroid function test measurement may be used as discriminative cut-offs between suicide attempters and healthy subjects. None of the thyroid hormones indicated future suicide attempts. Higher FT4, TSH, and lower FT3/FT4 levels are independently associated with suicide attempt. FT4 may be a useful marker to predict current suicide attempt.

Keywords: suicide attempt, suicide prediction, thyroid hormones, TSH

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## **INTRODUCTION**

Suicide is a complex matter concerning a number of psychological, biological, social, and cultural factors. In today's world, suicide is an important public issue, as well as one of the leading causes of death<sup>1</sup>. Therefore, understanding the causes of suicide and suicide attempts is quite valuable for public health regarding prevention of future attempts.

Suicide attempts differ with regard to gender. Women attempt suicide more often than men, but aggressive suicide attempts are higher in men than women<sup>2</sup>. It is known that thyroid hormone measurements do not change significantly between the genders, however, thyroid disorders are seen more frequently in women<sup>3</sup>. Studies suggest that thyroid hormones might be associated with many psychiatric diseases including suicide attempts<sup>4-7</sup>, but none examined their findings with regard to gender difference. Also, studies exploring the relationship between thyroid hormones, depression, and suicides were performed<sup>4,5</sup>. Therefore, thyroid hormone levels in suicide attempters according to gender differences was evaluated.

The primary aim of this study was to examine whether suicide attempters in Emergency Room were different from healthy controls with regard to thyroid hormones, namely FT3, FT4 (thyroxin), and TSH in all groups and also between females and males distinctly. The secondary aim was to determine if any of the thyroid hormone levels may have predicted current or future suicide attempts.

## **METHODS**

#### **Study Design**

This is a case control and clinical cohort study conducted in Ataturk University, Medical Faculty, Yakutiye Research Hospital.

#### Setting and participants

The study included suicide attempters who were admitted consecutively to the Emergency Room

(ER) of our university hospital during the day between November 2009 and December 2013. The control group consisted of healthy subjects who were admitted consecutively to check-up unit (generally for taking a health report which is often necessary to apply for a job in our country) where all thyroid hormones are routinely screened in daytime. A total of 358 (115 suicide attempters and 243 controls) subjects were included. All suicide attempters who were admitted in the ER and controls were evaluated according to DSM IV-TR criteria by a senior and experienced psychiatry resident and physical examination was conducted by an ER physician. Details of previous and current medical and psychiatric history within the last 6 months which included: current suicide attempt, previous suicide attempts, family history of psychiatric diagnoses and suicide attempts, were recorded by means of a semi-structured interview (exploring the reasons of the suicide attempts, existence of previous suicide plans, background motivation of suicide behavior, the feelings and motivation during suicide attempt, features of the suicide attempt (impulsive, preplanned, etc.), future suicide plans, the severity of the suicide, methods used in suicide attempts (self-poisoning, hanging, using firearms, etc.) and severity of death wish, etc.) and a review of medical records.

Suicide was defined as a conscious intent of a person to end his/ her own life and a suicide attempt was defined as a self-destructive action with some intent to die<sup>8</sup>. All suicide attempts in this study were labelled as type II (a self destructive action with some degree of purpose to end one's life and some identifiable injuries) according to the terminology<sup>9,10</sup>. All suicide attempters in this study declared that they really intended to die during the suicide attempts.

The study protocol was approved by local ethics committee and each subject provided written informed consents.

#### **Inclusion criteria**

Being  $\geq$  16 years of age for both groups. Admission to the emergency department at daytime hours

(08:00-17:00) because of the limited opening hours of check-up unit (where thyroid hormones are measured routinely) and assumed nyctohemeral secretion profile of TSH.

#### **Exclusion criteria**

The control and study groups including previous history of any thyroid disorder or chronic disease (endocrinological, pulmonary, gastrointestinal, neurological, infectious and neoplastic diseases, hepatic, renal or cardiac failure) that may affect thyroid hormone levels, use of any thyroid hormone or drug that may affect thyroid hormone levels, (such as lithium, carbamazepine, oral contraceptives, etc.) alcoholism or drug abuse other than nicotine, pregnancy, detected possible thyroid disease during procedure, intellectual disability, rejection of blood tests were excluded. For only controls, lifetime history of suicide attempt, current suicidal ideation, and previous or current psychiatric diagnosis were excluded. A total of 287 patients with suicide attempts were excluded because of admission at night (17:00-08:00) hours (246) and 41 for having exclusion criteria.

#### **Hormonal Analysis**

Approximately 5 ml of venous blood was collected and placed in a vacuum tube without additives. The blood samples of the suicide attempters who were admitted in ER during daytime were obtained within the first hour of initial visit to the ER. The blood samples of the controls were taken during daytime at the check-up unit. All the blood samples were collected during daytime (08:00-17:00) because of the limited opening hours of check-up unit and assumed nyctohemeral secretion profile of TSH4. A competitive chemiluminescent immunoassay (CLIA) was used to identify FT3 concentrations, sequential CLIA for FT4 concentrations and a two-site (sandwich) CLIA for TSH. An experienced endocrinologist evaluated the thyroid hormone levels. According to the evaluations, possible pathologic results related to

primary thyroid disease were excluded. Thyroid functions were evaluated by measuring plasma TSH, FT3, and FT4 levels. All participants were clinically euthyroid within the reference range of serum levels of FT3, FT4 and TSH. Normal ranges of laboratory kits that we used in this study were for TSH 0.27-4.2  $\mu$ u/ml for FT3 1.8-4.4 pg/ml for FT4 0.9-1.7 ng/dl. Free levels of T3 and T4 were measured because of the changing effect of the levels of thyroid hormone-binding serum proteins on total T4, even though levels of active FT4 may be unchanged<sup>11,12</sup>.

#### Follow-up

Using our hospital database and the database of the Republic of Turkey Social Security Institution, via International Classification of Diseases (ICD) diagnostic codes related to suicide data of future suicide attempts of the study participants was collected. The Social Security Institution can retrieve any medical records of Turkish citizens who have been admitted in any Health institution, including private medical institutions. Average follow-up period was 874.2 days, the longest follow-up period was 1,582 days for the first suicide attempter included in the study and the shortest follow-up period was 64 days for the last suicide attempter included in the study.

#### **Statistical Analysis**

All data were reported as the mean±SD or as n (%). Analysis of variance (ANOVA), chi-square test, independent samples t-test, Mann Whitney U test, and Kaplan Meier analysis were used for the comparisons when appropriate. Post-hoc comparisons of the groups were carried out using the LSD test. Binary logistic regression analysis was performed to determine the independent predictors for suicide attempts. Multivariate logistic regression analyses with backward elimination method were performed for statistically significant thyroid hormone measures. ROC curve analysis and cut off points for thyroid hormones were calculated. Area under the curve (AUC) was measured in the suicide attempt group. The analyses were performed using the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL) Version 20 for Windows. A result of p<0.05 was accepted as significant.

### RESULTS

### Sociodemographic characteristics of suicide attempters vs. healthy controls

A total of 358 (115 suicide attempters and 243 controls) subjects were included. Characteristics of the study participants are presented in Table 1.

Of the suicide attempters, 110 participants attempted suicide only by self-poisoning with drugs, 5 used violent attempts such as firearms (n=1), cutting a vein (n=3), and jumping off a high place (n=1). Two out of these five people took drugs at the same time. There was no in-hospital mortality. Collecting time of blood samples from suicide attempters and controls were similar.

According to DSM-IV criteria and psychiatric examination by a senior psychiatry resident and consulted to a specialist in ER; of the female suicide attempters, 30 patients were diagnosed as adjustment disorder, 45 mood disorders (43 depressive disorders, 2 bipolar affective disorder), 6 anxiety disorders, 2 schizophrenia and other psychotic disorders, 1 personality disorder. Of the male suicide attempters, 13 diagnosed as adjustment disorder, 15 mood disorders (14 depressive disorders, 1 bipolar affective disorder), 2 anxiety disorders, 1 schizophrenia and other psychotic disorders, 4 personality disorder and 4 could not have a certain diagnosis in ER. As a whole group 57 suicide attempters (49%) was diagnosed as depressive disorders (43 females, 14 males) and 8 were diagnosed as anxiety disorder (6 females, 2 males). Some of the suicide attempters in both female and male groups had comorbid psychiatric diagnoses. Differences between suicide

Characteristics	Female			Male		
	Suicide (n=78)	Controls (n=106)	р	Suicide (n=37)	Controls (n=49)	р
Average age	25.12±11.93	26.24±6.61	0.34	27.57±10.88	26.82±6.95	0.75
Body Mass Index	20.38±3.72	19.94±2.97	0.64	24.13±4.75	23.86±4.12	0.82
Married/single/other	26/44/8	34/67/5	0.33	11/24/2	12/33/4	0.81
Education* ↓M vs ↑M	35/43	27/79	0.008	14/23	3/46	0.0007
Employed/unemployed/student	8/42/28	12/34/50	0.048	17/10/10	18/4/27	0.011
Living in rural area/city center	13/65	12/94	0.4	11/26	6/43	0.08

#### Table 2: Thyroid hormone levels of the suicide attempters and controls

Gender		Control		Suicide attempt		р
	Hormone —	n	Mean±SD	n	Mean±SD	
Female	FT3 (pg/ml)	127	2.90±0.52	78	2.97±0.57	0.38
	FT4 (ng/dl)	165	0.98±0.22	78	1.33±0.32	< 0.001
	TSH (μιu/ml)	176	1.67±0.85	75	2.00±1.28	0.016
	FT3/FT4	100	3.13±0.87	74	2.25±0.75	<0.001
	FT3/TSH	100	2.41±1.73	70	2.11±1.81	0.2
	FT4/TSH	163	0.78±0.57	71	1.30±2.16	0.006
Male	FT3	57	3.17±0.55	37	3.19±0.57	0.94
	FT4	69	1.07±0.25	38	1.44±0.36	< 0.001
	TSH	72	1.50±0.89	37	1.88±1.24	0.06
	FT3/FT4	50	3.15±0.81	36	2.36±0.59	< 0.001
	FT3/TSH	51	2.88±1.66	35	2.73±2.58	0.74
	FT4/TSH	68	0.97±0.56	36	1.22±1.11	0.12

Table 3: Multivariate logistic regression analysis results for comparing patients with suicide attempters vs. controls					
Variables Total (n= 250)	OR	95% CI	Wald $\chi^2$ test(all df= 1)		
FT4	32.7	5.3 to 202.9	14.0 (p<0.0001)		
TSH	1.7	1.2 to 2.3	9.7 (p=0.002)		
FT3/FT4	0.4	0.2 to 0.8	7 (p=0.008)		
Variables entered on the logistic regression an described. CI: confidence interval; OR: odds rat		bles are selected using a backward selection	on procedure, and only significant (p< 0.05) are		

attempters with adjustment disorder and depressive disorder were not statistically significant in terms of thyroid functions. On admission, 38 females were frequently taking antidepressant drugs SSRIs, 13 were on antipsychotic treatment, and 2 were taking valproic acid. Nine males were on antidepressant treatment SSRIs, 3 were taking antipsychotic drugs, and 2 were on valproic acid medication.

## Thyroid hormone levels of suicide attempters vs. controls

Suicide attempters had statistically significantly higher FT4 and TSH levels and lower FT3/FT4 levels compared to healthy controls (Table 2). When thyroid function parameters which were found statistically significant in univariate logistic analysis were entered into the multivariate logistic regression analysis, it was seen that suicide attempters were 32.7 times more likely to have higher FT4 levels (OR: 32.7; 95% CI: 5.3-202.9; p<0.0001), 1.7 times more likely to have higher TSH levels (OR: 1.7; 95% CI: 1.2-2.3; p=0.002) and 2.5 times more likely to have lower FT3/FT4 levels (OR: 0.4; 95% CI: 0.2-0.8; p=0.008) than controls (Table 3).

## Thyroid hormone levels in suicide attempter subgroups

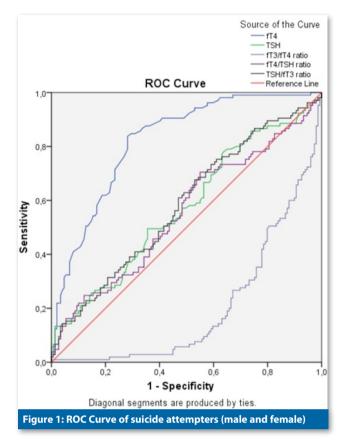
Suicide attempters subgroups were as follows: Eighteen patients (15.8%) had previous suicide history (n=9 (11.7%) F, n=9 (24.3%) M), 8 patients (7%) had a family history of suicide attempt (n=5 (6.5%) F; n=3 (8.1%), 35 patients (30.4%) had previous psychiatric diagnosis (n=23 (29.9%) F, n=12 (32.4%) M), 75 patients (65.2%) had at least one psychiatric referral in their lifetime (n=50 (43.5%) F, n=25 (21.7%) M), 37 patients (32.5%) had been consulted a psychiatrist in the last 6 months (n=22 (28.6%) F, n=15 (40.5%) M), 14 patients (12.3%) had a family history of psychiatric illness (n=8 (10.4%) F, n=6 (16.2%) M).

When the above subgroups were analyzed in terms of TFT (thyroid function tests), a significant difference was observed on just these subgroups: TSH levels of female suicide attempters who were admitted in a psychiatry clinic within the previous 6 months were significantly higher (n=21, TSH=2.5 vs. n=54, TSH=1.8, Mann-Whitney U test, p=0.025) than non-admitters. FT4 levels of male suicide attempters who were admitted in a psychiatry clinic within the previous 6 months were significantly lower (n=16, FT4=1.3 vs. n=22, FT4=1.6, Mann-Whitney U test, p=0.04) than nonadmitters. Males with previous suicide attempt had lower FT3 and FT4 levels (n=13, FT3=2.98 vs. n=24, FT3=3.3, p=0.072) (n=13, FT4=1.29 vs. n=25, FT4=1.51, p=0.085) than males without previous suicide attempt(s), but did not reach statistical significance. There was no significant difference among females.

We also evaluated the thyroid hormone levels of suicide attempters according to psychiatric diagnosis only between suicide attempters with depression and adjustment disorder because of the inadequate number of suicide attempters having other psychiatric diagnosis. No difference was detected between groups on both females and males.

#### Predicting current suicide attempters

In the ROC curve analysis on both male and female suicide attempters, FT4 levels were found as the most associated factor with suicide predictability



(Figure 1). Also its sensitivity to discriminate suicide attempters from controls was found as 82% (Table 4). A FT4 cut off point of 1.15 ng/dl was the most sensitive (85%) and specific (70%) level to discriminate suicide attempters from healthy controls regardless of gender (Table 5). The FT3/ FT4 level was also significant in the ROC analysis but with a very low AUC (Table 4).

# Role of thyroid hormones to predict future suicide attempt

We assessed that 64 suicide attempters were readmitted in our psychiatry outpatient clinic (56.1%, F n=45, 58.4%, M n=19, 51.4%) during follow-up. Health insurance data of our country showed that 13 of the suicide attempters (10 females, 3 males) reattempted suicide. None of the levels of thyroid function tests were different between suicide re-attempters and controls. Of these, 8 (5 females, 3 males) suicide re-attempts occurred during the first year of follow-up. None of

Gender	Parameter	AUC	SE	% <b>95 Cl</b>	р
Female+Male	FT4	0.821	0.026	0.77-0.872	<0.0001
	TSH	0.572	0.037	0.50-0.644	0.051
	FT3/FT4	0.202	0.027	0.148-0.256	< 0.0001
Female	FT4	0.832	0.31	0.771-0.893	< 0.001
	TSH	0.545	0.045	0.456-0.633	0.321
	FT3/FT4	0.203	0.034	0.137-0.269	< 0.001
Male	FT4	0.803	0.047	0.710-0.895	< 0.001
	TSH	0.623	0.065	0.496-0.751	0.054
	FT3/FT4	0.205	0.049	0.109-0.301	< 0.001

Hormone	Population	Cut-off Value	Sensitivity (%)	Specificity (%)	LR+	LR-
FT4	Female+Male	1.15	85	70	2.87	0.22
		1.37	43	89	3.99	0.64
	Female	1.18	81	76	3.35	0.24
		1.33	49	90	4.81	0.57
	Male	1.24	80	74	3.08	0.27
		1.44	40	94	6.67	0.64
SH	Female+Male	1.06	80	32	1.17	0.63
		1.94	37	71	1.29	0.88
	Female	1.10	80	34	1.22	0.58
		2.05	34	66	1.0	1.0
	Male	0.96	80	26	1.08	0.77
		1.89	40	82	2.22	0.73

the levels of thyroid function tests were different between participants who re-attempted suicide during first year follow-up and those who did not.

## DISCUSSION

Our research is one of the pioneering studies in the context of evaluating male and female suicide attempters together and separately with regard to suggesting thyroid hormone levels as biological marker(s) for suicide attempt. Including clinical euthyroid participants with normal FT3, FT4, and TSH serum levels, we showed that significant differences in thyroid hormones, particularly FT4 and TSH, do occur in suicide attempters. Regardless of gender, FT4 levels were found as the most associated factor with suicide predictability and the strongest component in differentiating suicide attempters from healthy controls. TSH levels of the female suicide attempters were significantly higher in female suicide attempters than controls and less significant in male suicide attempters.

Most of the suicide attempters (57 of 115) in our study were diagnosed as depressive disorders compatible with the literature findings. Different results regarding thyroid hormone levels in suicide attempters with psychiatric diagnosis were presented. In a study including 95 patients with major depressive disorder (53 patients were recent or past suicide attempters, 42 patients were nonattempters) and healthy controls basal TSH levels did not differ between groups. Patients with a positive suicide history had lower basal FT4 levels than controls and patients with negative suicide history<sup>4</sup>. Researchers declared that the results were possibly related to the upregulation of TSH by stress and stress hormones which may lead to an increase on T4 levels<sup>4</sup>. In another study 439 patients suffering from major depressive disorder, bipolar disorder and psychotic disorder suicide attempters were found to have lower FT3 levels than non-attempters but similar FT4 and TSH levels<sup>13</sup>. On female inpatients with unipolar depression, suicidal intent and agitation were found to be independently associated with lower

TSH response and patients with constant suicidal ideation could have low TRH messenger-RNA levels, suggesting diminished hypothalamic TRH drive to prompt TSH production and storage in pituitary, which might be precipitated by hypercortisolemia<sup>14,15</sup>. Also higher T4 levels, regardless of normal TSH levels, may rather be temporary because of the stress response associated with the suicide<sup>16</sup>.

In a study with depressed women, lower TSH response to TRH has been associated with violent suicide attempts and increased risk of suicide<sup>17,18</sup>. Our study included mostly nonviolent suicide attempters; this might be the reason for higher TSH in suicide attempters than controls. TRH hypersecretion might be a compensatory mechanism to continue normal thyroid hormone secretion and establish serotonin activity<sup>19</sup>. Also TRH hypersecretion might be the cause of high TSH in suicide attempters regardless of FT4 levels. In the case of a decrease in FT4 levels, TSH level is expected to increase and vice versa. In suicide attempters this mechanism may not be effective enough and this might play a role in the sustained serotonin hypoactivity steadily linked to suicide<sup>6</sup>. Our findings simultaneously suggested higher FT4 and TSH levels in suicide attempters than controls might be because of these complex and deteriorated association between the hypothalamic-pituitarythyroid (HPT) axis and thyroid hormones.

We found that twenty (17.4%) of the current suicide attempters had previous suicide attempts and during follow up 13 of them re-attempted suicide (11.3%). No parameter was found as related with predicting current suicide attempt according to previous attempt and predicting future suicide attempt according to current suicide attempt. FT4 levels were found as near significant. This finding should be paid careful attention.

We found that TSH levels of female suicide attempters with a diagnosis of mostly depression/ anxiety disorder who were admitted in a psychiatry unit within the previous 6 months were significantly higher than non-admitters. FT4 levels of male suicide attempters who were admitted to a psychiatry unit with mostly diagnosis of major depression/ anxiety disorder within the previous 6 months were significantly lower than those who were not. In a research evaluating personality traits of the suicide attempters, a positive relation between T4 levels and major depression/ anxiety disorder traits was found<sup>20</sup>. We assume that this finding might reflect the insufficient response to TSH or HPT axis deterioration in this group and may be different among males and females.

We could not find any significant differences with regard to FT3 levels between male and female suicide attempters and controls. While Pompili found suicide attempters 2.27 times less likely to have higher FT3 levels<sup>13</sup>, Duval detected no difference in suicide attempters compared to controls<sup>4</sup>. Thus, we suggest that the number of participants in our study could not be enough to detect differences or FT3 may not be a good predictor on predicting suicide attempts.

We found FT3/FT4 levels lower in suicide attempters than controls. This might be the result of increased FT4 levels in the peripheral tissue. In a study, aggressiveness was found to be negatively associated with the T3/T4 ratio<sup>21</sup>. If we presume suicide attempt itself as an aggressive behavior, we may say that our results are consistent with this study and a lower FT3/FT4 ratio might be important in suicide neurobiology. Also lower FT3/FT4 ratio might indicate the deficit in degradation of FT4 to FT3 in peripheral tissues in suicide attempters.

We suggest that a cut-off point of 1.15 ng/dl FT4 might have a good sensitivity (85%) and specificity (70%) on predicting current suicide attempters in both genders. This might be important for clarifying possible suicide attempts and situations on which obvious account of an event history could not be taken such as unintended drug poisoning, traffic accidents, falling off a high place, and etc. Another sign of suicide on these groups might be the increase of FT4 and TSH together. Also, these might be indicators of current, but not future, suicide attempts.

In our research FT4 levels above 1.44 for males showed moderate increase in the likelihood of suicide attempts. All other hormone levels had small increase in the likelihood of suicide attempts. The predicted capability of the model was assessed with an area under the curve model. The area under the ROC curve of FT4 for the prediction of suicide was 0.82. In terms of different genders area under the ROC curve of FT4 for the prediction of suicide was 0.83 for females and 0.8 for males. These findings supported that FT4 might have been the strongest hormone related to suicide attempt.

In this present study, we declare certain limitations. First, the small sample size and carrying out research in a single study center. Second, the ER assessment did not include a psychometric instrument to measure suicide severity and future suicide risk. Third, suicide attempters consisted mainly of non-violent attempters, due to cooperation difficulties with patients with violent attempts. Hence, our findings, which include unsuccessful suicide attempters only, can not be generalized to all kinds of suicide attempts. Fourth, stress would be an important confounding factor between study group and controls. In a study between psychiatric patients with suicide attempts and non-attempters FT4 and TSH levels were similar<sup>13</sup>. Also, there was some missing data. The reasons for missing data of some participants were lack of laboratory kits and unintentional forgetting to report thyroid hormone levels. We did not measure TRH, cortisol levels and thyroxin binding globulins. Also, we could not take the suicide attempters homogenously according to psychiatric diagnosis. A study including depressed patients with suicide attempts and without suicide attempts and healthy controls, found no difference on basal TSH, FT3 and FT4 levels with different psychiatric diagnosis<sup>4</sup>. Also in an other study including patients with major depression, bipolar disorder, schizophrenia, schizoaffective disorder, psychosis not otherwise specified; the effect of the different diagnosis on thyroid hormone levels were found as very weak<sup>13</sup>. We should also remark that the followup was period based on Turkey's Social Security Institution data. This data may include misdiagnoses or suicide attempts that did not intend to die.

In conclusion, our results suggest that some thyroid hormones might be dysregulated in suicide attempters.

### **References:**

- Altindag A, Ozkan M, Oto R. Suicide in Batman, southeastern Turkey. Suicide Life Threat Behav 2005;35(4):478-82. [CrossRef]
- Wiedenmann A, Weyerer S. The impact of availability, attraction and lethality of suicide methods on suicide rates in Germany. Acta Psychiatr Scand 1993;88(5):364-8. [CrossRef]
- Tunbridge WM, Evered DC, Hall R, Appleton D, Brewis M, Clark F, et al. The spectrum of thyroid disease in a community: the Whickham survey. Clin Endocrinol (Oxf);1977;7(6):481-93. [CrossRef]
- Duval F, Mokrani MC, Lopera FG, Diep TS, Rabia H, Fattah S. Thyroid axis activity and suicidal behavior in depressed patients. Psychoneuroendocrinology 2010;35(7):1045-54. [CrossRef]
- Duval F, Mokrani MC, Monreal J, Weiss T, Fattah S, Hamel B, et al. Interaction between the serotonergic system and HPA and HPT axes in patients with major depression: implications for pathogenesis of suicidal behavior. Dialogues Clin Neurosci 2002;4(4):417.
- 6. Mann JJ, Currier D. A review of prospective studies of biologic predictors of suicidal behavior in mood disorders. Arch Suicide Res 2007;11(1):3-16. [CrossRef]
- 7. Rich CL. Endocrinology and suicide. Suicide & lifethreatening behavior 1986;2(16):301-11. [CrossRef]
- Asberg M, Traskman L, Thoren P. 5-HIAA in the cerebrospinal fluid. A biochemical suicide predictor? Arch Gen Psychiatry 1976;33(10):1193-7. [CrossRef]
- Silverman MM, Berman AL, Sanddal ND, O'Carroll PW, Joiner TE. Rebuilding the tower of Babel: a revised nomenclature for the study of suicide and suicidal behaviors. Part 1: background, rationale, and methodology. Suicide Life Threat Behav 2007;37(3):248-63. [CrossRef]
- Silverman MM, Berman AL, Sanddal ND, O'Carroll PW, Joiner TE. Rebuilding the tower of Babel: a revised nomenclature for the study of suicide and suicidal behaviors. Part 2: suicide-related ideations, communications, and behaviors. Suicide Life Threat Behav 2007;37(3):264-77. [CrossRef]
- 11. Bayer MF, McDougall IR. Radioimmunoassay of free thyroxine in serum: comparison with clinical findings and results of conventional thyroid-function tests. Clinical Chemistry 1980;26(8):1186-92.

- 12. Schlienger JL, Sapin R, Demangeat C. La thyroxine libre. Concours Med 1983;105:5241-52.
- Pompili M, Gibiino S, Innamorati M, Serafini G, Del Casale A, De Risio L, et al. Prolactin and thyroid hormone levels are associated with suicide attempts in psychiatric patients. Psychiatry Res 2012;200(2-3):389-94. [CrossRef]
- Corrigan MH, Gillette GM, Quade D, Garbutt JC. Panic, suicide, and agitation: independent correlates of the TSH response to TRH in depression. Biol Psychiatry 1992;31(10):984-92. [CrossRef]
- Alkemade A, Unmehopa UA, Brouwer JP, Hoogendijk WJ, Wiersinga WM, Swaab DF, et al. Decreased thyrotropinreleasing hormone gene expression in the hypothalamic paraventricular nucleus of patients with major depression. Mol Psychiatry 2003;8(10):838-9. [CrossRef]
- Prange AJ Jr. Thyroid axis sustaining hypothesis of posttraumatic stress disorder. Psychosom Med 1999; 61(2):139-40. [CrossRef]
- 17. Linkowski P, Van Wettere JP, Kerkhofs M, Brauman H, Mendlewicz J. Thyrotrophin response to thyreostimulin in affectively ill women relationship to suicidal behaviour. The British Journal of Psychiatry 1983;143(4):401-5. [CrossRef]
- Linkowski P, Van Wettere JP, Kerkhofs M, Gregoire F, Brauman H, Mendlewicz J. Violent suicidal behavior and the thyrotropin-releasing hormone-thyroid-stimulating hormone test: a clinical outcome study. Neuropsychobiology 1984;12(1):19-22. [CrossRef]
- Duval F, Mokrani MC, Bailey P, Correa H, Diep TS, Crocq MA, et al. Thyroid axis activity and serotonin function in major depressive episode. Psychoneuroendocrinology 1999;24(7):695-712. [CrossRef]
- 20. Arque JM, Segura R, Torrubia R. Correlation of thyroxine and thyroid-stimulating hormone with personality measurements: a study in psychosomatic patients and healthy subjects. Neuropsychobiology 1987;18(3):127-33. [CrossRef]
- Stalenheim EG. Long-term validity of biological markers of psychopathy and criminal recidivism: follow-up 6-8 years after forensic psychiatric investigation. Psychiatry Res 2004; 121(3):281-91. [CrossRef]