

# Is there a relationship between thyroid hormone levels and suicide attempt in adolescents?

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## Abstract

**Background:** Thoughts about suicide are quite common in adolescent. While such thoughts can be caused by many reasons, the most well-known of these are mood disorders. There are studies related to coexistence of thyroid pathologies and mood disorders in adult. **Objectives:** In this study, we aimed to investigate the difference of thyroid hormone levels in between adolescents with suicide attempt history and normal population. **Methods:** The study was prospective and was designed as a case-control study. Demographic characteristics of the patients were obtained and Serum fT3, fT4 and TSH levels were examined. **Results:** 222 cases were included in the study, including 101 cases and 121 controls. As for TSH levels, the mean serum levels of the whole group was  $1.96 \pm 1.08$  mU/L, while the mean serum levels of the control group was  $2.33 \pm 1.5$  mU/L and the mean serum levels of the case group was  $0.50 \pm 0.3$  mU/L which revealed that the mean serum levels of the case group was significantly lower ( $p < 0.01$ ). **Conclusion:** It was found that serum TSH levels were significantly lower in case group than control group and the individuals with subclinical hyperthyroidism had more suicide attempts than the ones in control group.

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## Introduction

Thoughts about suicide are quite common in adolescent age group. In a study conducted in the USA in 2011, it was found that 13% of all adolescents had a suicide planning and 8% of them had a suicide attempt during one year. However, the completed suicide attempt is quite rare<sup>1,2</sup>. According to the 2012 data of Turkish Statistical Institute, despite the fact that the raw suicide rate in our country is determined as 3.62, it is impossible to know the certain number since all cases are not reported<sup>3</sup>. Despite the rareness of resulting in death of these suicide attempts, the problems related to the disengagement from the educational life of the cases and the morbidity caused by the suicide attempt they have had, are important on every individual basis. In addition, the increase in the workload of emergency services and the increase in health expenditures also pose a national problem. Therefore, it would be a reasonable approach to determine the factors that may lead to suicide attempts and to take protective measures against these factors.

When we evaluate the risk factors of a suicide attempt, having a history of suicide attempt by the individual or one of their family member, having a sexual identity disorder (gay, lesbian, bisexual orientation, transgender identity), having a history of child abuse and having one or multiple of mood disorders (major depression, substance use disorders, psychotic disorders) can be encountered<sup>4</sup>.

Many of these risk factors are social problems that cannot be cured by physicians. Separately from the other factors, mood disorders can be diagnosed and treated and this gives physicians an opportunity to prevent a serious problem such as suicide attempt.

Genetic factors, stressful conditions, inadequate social support, substance use, and various somatic diseases can be observed in the etiology of mood disorders<sup>5</sup>. Also, mood disorders may develop secondarily to several disorders, such as neurological diseases (Epilepsy, Parkinson's Disease, Cerebrovascular diseases), infectious diseases (HIV, neurosyphilis), endocrine disorders (hypothyroidism, diabetes mellitus, parathyroid hormone disorders), and some vitamin deficiencies<sup>6</sup>.

From this point of view, we aimed to investigate the effect of thyroid dysfunction, which is one of the correctable endocrinopathies that may cause mood disorders, on a suicide attempt.

## Methods

This study was carried out between 01.01.2017-31.12.2017 in a pediatric emergency department of a tertiary university hospital in the city center. The study was designed as a case-control study. The approval of the regional ethics committee was obtained, and the signed informed consent form was obtained from the legal guardian of the participants.

## Cases

The study group consisted of girls between 14-18 age (According to WHO's age classification, between 10-19 age is called as "adolescent age period" and between 14-24 age is called "young people". Therefore, we formed young and adolescent age groups in our study) who admitted to the pediatric emergency department with suicide attempt and who accepted to participate in the study. The control group consisted of the patients who admitted to healthy child clinic with similar age, gender, and ethnic characteristics but unknown thyroid hormone levels. Age, gender and ethnic origins of the study group were obtained. The psychiatric evaluation was made by a specialist on child and adolescent psychiatry for those who attempted suicide. No psychiatric evaluation was made on control group but asked about the previous diagnoses for psychiatric diseases. The individuals in doubt of any psychiatric disorders were excluded from the control group. Patients using any agent that could alter the thyroid axis and/or metabolism, those lacked data, and those who did not agree to participate in the study were excluded from the study. Pregnancy status was confirmed with serum  $\beta$ -hCG levels in addition to the statement of expression, and those with gestational status were excluded from the study.

## Laboratory Analysis

Blood samples of the cases were taken between 8-10 am and were sent to the laboratory. The samples were run without delay. All hormonal concentrations were determined by immunoassay techniques based on enhanced Lumine sense. Normal levels of thyroid hormones are affected by many factors such as age, race, sex, chronic diseases, blood lipid levels, and nicotine use. Therefore, changes may be observed between the reference values in clinical use. In our study, we used the values given for girls between the ages of 12 and 19 as reference values in the National Health and Nutrition Examination Survey (NHANES) 2007-2012 study. According to this report, normal ranges were stated as 0.6-3.2  $\mu$ IU / ml for TSH, 3-4.3 pg/ml for free T<sub>3</sub> (fT<sub>3</sub>) and 0.6-1ng / dl for free T<sub>4</sub> (fT<sub>4</sub>).<sup>7</sup> Patients with low fT<sub>4</sub> levels, normal or low levels of fT<sub>3</sub> levels and high levels of TSH compared to the mentioned reference values, accepted as 'primary hypothyroidism'. Patients with low levels of TSH and high or normal levels of fT<sub>4</sub> and high levels of T<sub>3</sub> are accepted as 'hyperthyroidism'. Patients with low levels of TSH and normal levels of fT<sub>4</sub> and fT<sub>3</sub> are classified as 'subclinical hyperthyroidism'. Patients with high levels of TSH and normal levels of fT<sub>4</sub> and fT<sub>3</sub> are classified as 'subclinical hypothyroidism'. Patients with normal values of T<sub>3</sub>, T<sub>4</sub> and TSH levels, are classified as 'euthyroidism'.<sup>7</sup>

## Statistical Analysis

In the light of previous studies, the minimum sample size was calculated as 162 cases (81 case + 81 control) with %80 power. All data were analyzed in SPSS 20.0 (SPSS Inc. Illinois, US) package program. Independent T test, Chi-square analysis were used for comparison between groups, relationship and predicting variables, respectively. The results were presented as mean (standard deviation) or numbers (%) where applicable. Kruskal Wallis test used for comparing more than two groups. The alpha-level of significance was set at  $p < 0.05$ .

## Results

A total of 222 cases were included in the study, including 101 cases and 121 controls. All of the participants were in female gender. The

mean age of the case group was  $15.6 \pm 1.2$  years and the control group had a mean age of  $16.04 \pm 1$  years ( $p = 0.1$ ). It was observed that the case and control groups consisted of similar patients in terms of age. It was found that 92 girls (91.1%) in the case group consisted of the resident population and 9 (8.9%) were immigrants. The control group consisted of 119 (98.3%) residents and 2 (1.7%) immigrants ( $p = 0.3$ ) (Table 1).

63 patients (62.4%) in the case group were diagnosed with psychiatric disorders by a pediatric psychiatrist. Among these, 36 (35.7%) were diagnosed with major depression (MD), 21 (20.8%) with impulsive disorder and 6 (5.9%) with generalized anxiety disorder (Table 2).

The mean serum T<sub>3</sub> level of the whole group was  $3.46 \pm 0.76$  pg/ml (0-5.2), the mean of the control group was  $3.43 \pm 0.3$  pg / ml (2.8-4.9), while the mean T<sub>3</sub> level of the case group was  $3.47 \pm 0.84$  (0-5.2) pg. / ml. (T = 0.18 and P=0.67 (T-Test))

The mean serum T<sub>4</sub> level of the whole group was  $0.9 \pm 0.22$  ng/dl (0.29-2.1), the mean of the control group was  $0.90 \pm 0.8$  ng/dl (0.6-2.1), while the mean T<sub>4</sub> level of the case group was  $0.9 \pm 0.25$  ng/dl (0.29-2.1). (T = 0.43 and P = 0.49 (Test))

The mean serum TSH level of the whole group was determined as  $1.96 \pm 1.08$  mU/L (0.1-5.5), the mean serum TSH level of the control group was  $2.33 \pm 1.5$  mU/L (0.6-5.5), while the mean TSH level of the case group was  $0.5 \pm 0.3$  mU/L (0.1-3.7). The mean TSH value of the case group was found to be significantly lower (T: 1.3 and P < 0.01 (T-Test) (Table 3).

According to the reference values in NHANES (2007-2012) study, in whole group serum fT<sub>3</sub> level was found to be low in 18 cases (15.9%), normal in 87 cases (78.6%) and high in 6 (5.5%) patients. fT<sub>4</sub> level was found to be low in 3 cases (1.4%), normal in 176 cases (80%) and high in 41 cases (18.6%). Serum TSH levels were found to be low in 194 (87.4%) cases, normal in 14 (6.3%) cases and high in 12 (5.4%) cases. No significant relationship was found between the case-control group and serum T<sub>3</sub> and T<sub>4</sub> levels ( $p: 0.07$  and  $p: 0.3$  (Kruskal-Wallis analysis)). TSH level was found to be significantly lower in the case group. ( $p: 0.02$  (Kruskal-Wallis analysis)) (Table 4).

Based on the thyroid status definitions we mentioned before, no cases were diagnosed as primary hypothyroidism, 12 cases (5.7%) (all 12 in the control group) were diagnosed as subclinical hypothyroidism, 6 cases (2.9%) (all 6 in the suicide group) were euthyroid, 39 cases (18.7%) (22 controls + 17 cases) were diagnosed as hyperthyroidism and 152 cases (72.7%) (77 controls + 75 cases) were diagnosed as subclinical hyperthyroidism. The number of patients diagnosed with subclinical hyperthyroidism were significantly higher in the case group ( $p < 0.01$ ) (Chi-square test) (Table 5).

## Discussion

Our study is the first study which investigates the relationship between thyroid function and suicide attempts in adolescent age group. According to this, it is found that in suicide group serum TSH levels were significantly lower than control group.

In addition, individuals with subclinical hyperthyroidism had more suicide attempts than the control group as a secondary result.

Considering the relationship between suicide attempt and thyroid function, studies in the adult group are noteworthy. Although the relationship between thyroid hormones and mood disorders has been studied on adults, which thyroid disease plays a role in the etiology of which psychiatric disease is not clear yet. It is known that, especially when negative symptoms are predominant, such as in depression, monoamine levels are found to be lower in cerebrospinal fluid (CSF). Some of the studies at the cellular level

Table 1. Gender, Ethnicity and Age Properties

	All cases (N=222) N%		Non-suicide control (N=121) N%		The cases who had suicide attempt (N=101) N%		p
Ethnicity							0.3
Inhabitant	211	95	119	98.3	92	91.1	
Immigrant	11	5	2	1.7	9	8.9	
Total	222	100	121	100	101	100	
Where do they live?							
With Family	182	78	119	91.5	63	62.4	0.4
Homeless	7	3.1	1	0.7	6	5.9	
Married	6	2.3	0	0	6	5.9	
Public shelter	10	4.5	1	0.7	9	8.9	
Unknown	27	12.7	10	7.1	17	16.9	
Total	222	100	142	121	101	100	
Age (year)							
Mean ± SD Min/max	15.8±1.1	14/18	16.04±1	14/17	15.6±1.2	14/18	0.1

Table 2. Properties Of Suicide Attempters

	N	%
Diagnosed psychiatric disorder	63	62.4
Major depressive disorder	36	35.7
Impulsive disorder	21	20.8
Generalized anxiety disorder	6	5.9
No- diagnosed psychiatric disorder	38	37.6
Total	101	100

Table 3. The Results of Student T test Analysed For Serum ft3, ft4 and TSH levels

	All Cases N=222 (Mean ± SD)	Non-suicide Control N=121 (Mean ± SD)	The cases who had suicide attempt N=101 (Mean ± SD)	P	T
Free T 3 (pg/ml)	3.46 ± 0.76	3.43 ± 0.30	3.47 ± 0.84	0.67	0.18
Free T 4 (ng/dl)	0.90 ± 0.22	0.9 ± 0.80	0.90 ± 0.25	0.49	0.43
TSH (mU/L)	1.96 ± 1.08	2.33 ± 1.5	0.50 ± 0.3	<0.01	1.3

Table 4. The Relationship Between Case-Control Groups And The Groups Classified by ft3, ft4 and TSH Levels (Kruskal-Wallis Analysis)

	All Cases (N = 222) N (%)		Non-suicide control (N = 121) N (%)		The cases who had suicide attempt (N = 101) N (%)		P
ft3							0.07
Low	18	15.9	3	13.6	14	13.9	
Normal	87	78.6	19	86.4	81	80.2	
High	6	5.5	0	0	6	5.9	
Total	108	100	22	100	104	100	
ft4							0.3
Low	3	1.4	0	0	3	3	
Normal	176	80	95	78.5	81	80.2	
High	41	18.6	24	19.8	17	16.8	
Total	220	100	119	100	101	100	
TSH							0.02
Low	194	87.4	99	81.8	95	94.1	
Normal	14	6.3	8	6.6	6	5.9	
High	12	5.4	12	9.9	0	0	
Total	220	100	119	100	101	100	

**Table 5.** The Relationship Between Case-Control Groups According To Thyroid Status (Chi Square Analyses)

	All Cases N = 209 N%		Non-suicide Control N=111 N%		The cases who had suicide attempt N=98 N%		P
Primary Hypothyroidism	0	0	0	0	0	0	-
Subclinical hypothyroidism	12	5.7	12	10.8	0	0	-
Euthyroidism	6	2.9	0	0	6	6.2	-
Hyperthyroidism	39	18.7	22	19.8	17	17.3	0.06
Subclinical hyperthyroidism	152	72.7	77	69.4	75	76.5	<0.01

that attempts to elucidate the etiology, indicates that this is related to low TSH levels. In a study that supports this hypothesis, high levels of TRH in CSF was found in patients with severe depressive symptoms<sup>8</sup>. For example, in a study investigating the mechanisms of suicidal behavior at the cellular level, it was reported that TRH overactivity stimulates 5-HT activity in depressed patients and shows a compensatory response to decreased 5-HT levels<sup>9</sup>. In another study investigating the mechanisms of suicidal behavior at the cellular level, 5-HIAA (Hydroxyindolacetic acid) and HVA (Homovanillic acid) levels were found to be lower in CSF<sup>10</sup>. In another study supporting the hypothesis that the elevation in TSH is involved in the etiology of mood disorders, a negative correlation is found between the maximum TSH response and the levels of HVA and 5-HIAA in CSF<sup>11</sup>. When the studies examining the clinical implications of these mechanisms are analyzed, it is observed that hypothyroidism is a risk factor for the patients who have dominant negative symptoms such as major depressive disorder. For example, Jokinen et al. found a negative correlation between T3 levels and depression scale in their study on the patients who had suicide attempt in Sweden<sup>12</sup>. Gold *et al.* also reported that hypothyroidism increases the risk of depression<sup>13</sup>. Frey et al. also showed coexistence between hypothyroidism and depression<sup>14</sup>.

Some studies suggest that hyperthyroidism increases suicidal thoughts in patients with psychosis. For example, Jose et al. reported that patients with schizophrenia had suicidal thoughts and that hyperthyroidism was a risk factor<sup>15</sup>. Similarly, Sinai et al. stated that higher T4 levels increases aggression and suicide attempts<sup>16</sup>. In a cohort study of 43,633 patients with hyperthyroidism retrospectively analyzed, Abraham-Nordling et al. stated that patients with hyperthyroidism have a 1.6-fold higher risk in terms of suicidal attempts<sup>17</sup>. Bauer *et al.* stated that 10% of individuals with hyperthyroidism had a psychiatric disorder<sup>18</sup>. The mechanism of this condition was explained by the fact that thyroid hormones increase the number and intensity of B-adrenergic receptors in both the peripheral and central nervous system, resulting in increased catecholaminergic activity<sup>19</sup>. It is also observed that the increase in excitatory neurotransmitters with over-activation of the sympathetic nervous system also triggers manic episodes, psychotic attacks and anxiety disorders<sup>17</sup>. Similarly with the above studies, we observed lower TSH levels in suicide group than in control group while fT<sub>3</sub> and fT<sub>4</sub> levels were normal in both groups. Subclinical hyperthyroidism was higher in case group than in control group while clinical hyperthyroidism was not.

In some studies, no relationship was found between thyroid status and direct suicidal behavior. For example, Duval et al. examined the thyroid axis in depressed patients who attempted suicide and reported that hormones belonging to the HPT (Hypothalamic Pituitary Thyroid) axis were found to be normal in the early period<sup>20</sup>.

## Conclusion

As a result, the exact relationship between thyroid status and suicidal attempts is not clear. The probable reasons are heterogeneity

of study groups, multiple factors that change thyroid hormone levels, and geographic location of the cases. However, the euthyroid condition will undoubtedly provide both mood stabilization and the unlikelihood of suicidal thought. From this point of view, in terms of preventive health measures, physicians who are interested in adolescent age group should ask for endocrinology consultation when they encounter abnormal values while they are assessing thyroid levels of patients. We believe that our study will contribute to the literature in this respect and think that it will lead to more studies.

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