A comparison for thyroid functions and clinical features in deficit and non-deficit schizophrenia

Ali İnaltekin[1], Yasin Taşdelen[2]
[1]Assist. Prof., Department of Psychiatry, Kastamonu Unıversity School of Medicine, Kastamonu, Turkey https://orcid.org/0000-0003-0933-0308
[2]M.D., Aydın State Hospital, Department of Psychiatry, Aydın, Turkey https://orcid.org/0000-0003-4985-0690

SUMMARY

Objective: The primary occurrence and persistence of negative symptoms observed in patients with schizophrenia is deficit syndrome. Although the association between thyroid hormones and schizophrenia symptoms has been reported, no studies have investigated thyroid function in patients with deficit schizophrenia (DS). This study aims to investigate the clinical features and thyroid function in DS patients by comparing them with patients with non-deficit schizophrenia (NDS) and a control group.

Method: 33 subjects from DS, 35 subjects from NDS and 35 healthy control subjects were included in the study. Patients with schizophrenia were classified into DS and NDS using the deficit syndrome table. Thyroid function was assessed by the levels of TSH, free T3 (fT3), and free T4 (fT4). Sociodemographic data and clinical characteristics were evaluated using the Sociodemographic Data Form, the Positive Symptoms Evaluation Scale (SAPS), the Negative Symptoms Evaluation Scale (SANS), and the Calgary Depression in Schizophrenia Scale (CDSS).

Results: There was no significant difference between DS and NDS groups in terms of age, gender, marital status and education ($p>0.05$). The percentage of unemployed was significantly higher in the DS group than in the NDS group ($p=0.005$). There were 14 (42.4%) suicide attempts in the DS group and 11 (31.4%) in the NDS group, and there was no significant difference between the groups ($p>0.05$). There was no significant difference between the groups when comparing the thyroid functions of the DS, NDS and healthy control groups regarding fT4, fT3 and TSH ($p>0.05$). There was no significant correlation between TSH, free T3, free T4 and total SANS, total SAPS and CDSS scores ($p>0.05$).

Discussion: According to our study thyroid function is not different in DS, NDS and healthy controls and is not associated with positive, negative and depressive symptoms in patients with schizophrenia.

Key Words: Schizophrenia, deficit syndrome, thyroid hormones, signs and symptoms

INTRODUCTION

Negative symptoms consist of emotional limitation, alogy, anhedonia, social decline and avolition (1). Nevertheless, negative symptoms are associated with significant functional disability, decreased quality of life, and increased care needs (2,3). These negative symptoms may be temporary or permanent. According to the source, they are classified as primary if they are related to schizophrenia, and secondary if they are due to another reason such as drug side effects, psychotic symptoms, depressive comorbidity, lack of stimuli (4). The presentation of primary and persistent negative symptoms in schizophrenia is called the schizophrenia deficit syndrome (5). This group of patients with deficit schizophrenia (DS) is thought to constitute one-third of patients with schizophrenia (6). Studies comparing the differences between the deficit schizophrenia group (DS) and the non-deficit schizophrenia group (NDS) contributed to the hypothesis that DS may be a distinct disorder (7,8). However, despite this evidence for deficit schizophrenia, it was not included as a subtype or a

DOI: 10.5505/kpd.2024.22309

Cite this article as: Inaltekin A, Tasdelen Y. A comparison for thyroid functions and clinical features in deficit and non-deficit schizophrenia. Turkish J Clin Psych 2024; 27:5-11

The arrival date of article: 04.08.2023, **Acceptance date publication:** 07.09.2023

Turkish J Clinical Psychiatry 2024;27:5-11

distinct psychotic disorder in the Fifth Diagnostic and Statistical Manual of Mental Disorders (9).

Although there is a neurohormonal effect in mental illnesses, it is difficult to confirm this role, especially in chronic diseases such as schizophrenia, since it is difficult to conduct hormonal studies that exclude the effect of drug use, the number of psychotic exacerbations, and the duration of the illness. In studies conducted patients with schizophrenia, abnormalities in the thyroid system such as decreased activity of the hypothalamo-pituitary-thyroid axis, increase in thyroid autoantibodies and decrease in T3 levels have been shown. (10). It has been shown that fT3 and fT4 levels are low and TSH is high in the chronic phase of schizophrenia (11). Although abnormalities in the thyroid system have been reported, there are not enough studies investigating abnormalities in the thyroid system in DS patients.

Less is known about the role of thyroid hormones in the pathophysiology of schizophrenia compared with the aforementioned endocrine disorders. It has been reported that clinically significant hyperthyroidism may occur in individuals with psychotic symptoms, and hypothyroidism may cause mood problems that resemble the negative symptoms of schizophrenia (12-14). Despite the association between thyroid hormones and symptoms has been reported, no studies investigate thyroid function in DS patients.

This study aims to investigate the clinical features and thyroid function in DS patients and compare them with NDS patients and healthy controls.

METHOD

Sample and study design

In this study, the patients in the patient group were selected from patients diagnosed with schizophrenia who presented to Aydin State Hospital Community Mental Health Center (CMHC) between December 2022 and April 2022. Patients with schizophrenia were categorized as DS and NDS using the Schedule for the Deficit Syndrome by the same psychiatrist. Two diagnostic methods are used for DS. 'Proxy for Deficit Syndrome' created using the Brief Psychiatric Rating Scale and the Positive and Negative Syndrome Scale and the 'Schedule for the Deficit Syndrome' (SDS) (15,16). The SDS was preferred in this study because it has inter-rater reliability, a high degree of stability with good test-retest reliability and it is the gold standard for the diagnosis of DS (17). The study included 33 individuals from DS, 35 from NDS, and 35 of similar age and gender as a healthy control group. Inclusion criteria for the patient groups were that they were between 18 and 65 years of age, had been in clinical remission for at least 3 months, had been taking a stable dose of antipsychotics for at least 12 months, and were clinically compatible with the scales to be used. Exclusion criteria for the patient and the healthy control groups were an additional diagnosis of a psychiatric disorder, chronic inflammatory disease, cancer or autoimmune disease that might affect thyroid function, mental retardation or cognitive impairment, and alcohol or drug use disorders.

Thyroid function data for the patient groups were obtained from routine CMHC applications. Sociodemographic data and scales were collected from patients when routine examinations were requested. Thyroid function data for the healthy control group were obtained from the examination results of individuals registered for screening at the internal medicine outpatient clinic of Aydin Adnan Menders University Faculty of Medicine Hospital. This study was conducted under the 1964 Declaration of Helsinki and its subsequent amendments. Ethical approval for the study was obtained from the Clinical Research Ethics Committee of the Aydin Adnan Menders University (Project number: E.278543).

Data Collection Tools

Sociodemographic Data Form: A questionnaire prepared by the authors was used to obtain information on patients' sociodemographic data, medications taken, duration and course of the disease.

Schedule for the Deficit Syndrome: It is a chart developed to detect deficiency syndrome. In the

first part, negative symptoms, consisting of limited affect, decreased emotional range, poor speech, lack of interest, a decreased sense of purpose, and decreased social drive, are scored between 0-4. For deficit syndrome, at least two symptoms must score 2 or higher. The second part assesses whether the negative symptoms from the first part have persisted within the past year. The third part assesses whether or not the negative symptoms are primary. The Turkish validity and reliability study was conducted by Çıtak et al. (18).

Positive Symptoms Evaluation Scale (SAPS): The scale consists of 34 items and 4 subscales: Hallucinations, Delusions, Strange Behavior, and Formal Thought Disorders. The severity of each item varies between 0-5. The Turkish validity and reliability study was conducted by Erkoç et al. (19).

Negative Symptoms Evaluation Scale (SANS): The scale consists of 25 items and 5 subscales: emotional blunted, alogia, decreased energy and desire, lack of pleasure, and social withdrawal and attention. The severity of each item varies between 0-5. Erkoç et al. investigated its Turkish validity and reliability (20).

Calgary Depression Scale in Schizophrenia (CDSS): It is a scale that assesses depressive symptoms in patients with schizophrenia independently of negative, positive symptoms and extrapyramidal side effects. It consists of 9 items, and the severity of each item varies between 0-3. Aydemir et al. (21) conducted Turkish validity and reliability studies. The cutoff score was reported as 11/12. In this study, it was taken as 11.

Statistical Analysis

The values of Skewness and kurtosis were checked for the normality test. Normal distribution was assumed if the values of kurtosis and Skewness were between -1.5 and +1.5. The t-test was used to compare the numerical values in the two groups, and the one-way ANOVA test was used to compare the numerical values in the three groups. The chi-square test was used to compare categorical data. Pearson correlation analysis was used for correlation analysis.

RESULTS

The DS group included 25 (75.8%) men and 8 (24.2%) women. The NDS group consisted of 23 (65.7%) men and 12 (34.3%) women, and the healthy control group consisted of 22 (62%, 9) men and 13 (37.1%) women. The mean age was 51.88±11.29 years in the DS group, 46.61±11.53 years in the NDS group, and 46.23±13.18 years in the healthy control group. There was no significant difference between the groups regarding gender and age (p=46.23±13.18 and p=0.104, respectively). 100% of the DS group were unemployed, 77.1% of the NDS group were not employed, and the percentage of unemployed was significantly higher in the DS group (p=0.005). The duration of illness was 25.73±12.57 years in the DS group and 20.14±10.42 years in the NDS group. The number of psychotic exacerbations was 5.42±3.51 in the DS group and 3.88±2.28 in the NDS group, with no significant difference between groups (p=0.05 and p=0.067, respectively). There were 14 (42.4%) suicide attempts in the DS group and 11 (31.4%) in the NDS group, and there was no significant difference between the groups. (p=0.347). (Table 1.)

When comparing the mean scale scores of the patients with schizopfrenia group's DS and NDS, the total and subscale scores of SANS (Assessment of Negative Symptoms) in the areas of emotional blunting, alogia, apathy, anhedonia, attention deficit at the significance level $p < 0.001$, the SAPS (Assessment of Positive Symptoms) subscale disorganized behavior blunted at the significance level p=0.018, and the CDSS blunted at the significance level p=0.017 was higher in the DS group. (Table 2.)

When comparing the thyroid functions of DS, NDS and the healthy control groups in terms of free T4 (fT4), free T3 (fT3) and TSH, there was no significant difference between the groups (p=0.093, p=0.398, p=0.647, respectively). (Table 3.)

There was no significant correlation between TSH, fT3, fT4 and total score SANS, total SAPS and CDSS score. There was a positive (r=0.284, p=0.019) significant correlation between SAPS total score and the SANS total score. There was a

Table 1. General characteristics of the participants

	Deficit	Non-deficit	Healthy control	P
Variable				
Age, mean–SD	51.88–11.29	46.61–11.53	46.23–13.18	0.104
Education (year), Mean–SD	7.58–3.77	9.14–3.95		0.1
Gender, Number (%)				
Men	25 (75.8)	23 (65.7)	22 (62,9)	0.491
Women	8 (24.2)	12 (34.3)	13 (37,1)	
Marital status, Number (%)				
Married	12 (36.4)	8 (22.9)		0.446
Single	15 (45.5)	18 (51.4)		
Divorced	6 (18.2)	9 (25.7)		
Working status, Number (%)				
Employed	0 (0)	8 (22.9)		0.005
Unemployed	33 (100)	27 (77.1)		
Durations of illness (year), Mean–SD	25.73–12.57	20.14–10.42		0.05
Psychotic exacerbations, Mean–SD	5.42–3.51	3.88–2.28		0.067
Suicide attempts, Number (%)				
Having attempted suicide	14 (42.4)	11 (31.4)		0.347
No suicide attempt	19 (57.6)	24 (68.6)		
Typical AP using, Number (%)				
Using	10 (30.3)	6 (17.1)		0.201
Not using	23 (69.7)	29 (82.9)		
Atypical AP using, Number (%)				
Using	28 (84.8)	33 (94.3)		0.252
Not using	5 (15.2)	2 (5.7)		
MD using, Number (%)				
Using	5 (15.2)	9 (25.7)		0.282
Not using	28 (84.8)	26 (74.3)		
AD using, Number (%)				
Using	11 (33.3)	16 (45.7)		0.297
Not using	22 (66.7)	19 (54.3)		
Smoking, Number (%)				
Smoker	18 (54.5)	24 (68.6)		0.234
Non smoker	15 (45.5)	11 (31.4)		

SD: Standard deviation, AP: Antipsychotic, MD: Mood stabilizer, AD: Antidepressant

positive correlation between the CDSS score ($r=0.498$ $p < 0.001$) and a positive correlation between the SANS total score and the CDSS score ($r=0.267$, $p=0.028$). (Table 4.)

DISCUSSION

This study assessed thyroid function in DS and NDS patients. There was no difference between the two groups and the healthy control group regarding TSH, fT3, and fT4. Moreover, it was found that these levels were not associated with negative, positive and depressive symptoms.

Although there are studies investigating thyroid functions in patients with schizophrenia, there are no studies investigating DS patients. In our study, thyroid function was assessed as TSH, fT3, and fT4 between the group's DS, NDS and the control group, and no significant difference was found between the groups. In a study conducted in our country, no significant difference was found in peripheral thyroid hormone levels (fT3, fT4) in schizophrenia with positive symptoms and schizophrenia with negative symptoms under the criteria reported by Andreasen and Olson (22,23). While positive and negative schizophrenia criteria were used in this study, we used SDS in our study. SDS is the gold standard for diagnosis of DS. For DS/NDS classification with SDS, it is recommended that patients be in periods of clinical stability (17). The patients in our study were also in clinical remission. Although other methods are used in terms of group (their groups: positive and negative schizophrenia, our groups: DS and NDS) formation, the results of our study are consistent with this study conducted in our country. However, the fact that our sample size was larger than this study and in our study there was no significant difference between the groups in terms of age, gender, type of drug used, number of psychotic exacerbations, and duration of illness makes our study stand out. The results of studies comparing patients with schizophrenia with the control group are inconsistent. Some studies found no difference in TSH (24,25), no difference in TSH and fT4 (26), no difference in TSH and fT3 (11) no difference in TSH

Table 2. Comparison of scale scores between groups

	Deficit Mean–SD	Non-deficit Mean–SD	P
Variable			
SAPS- hallucinations	3.00–4.76	1.86–3.45	0.260
SAPS-delusions	9.30–6.70	7.00–5.61	0.265
SAPS- disorganized behavior	4.97–2.05	3.69–2.28	0.018
SAPS- formal thought disorders	2.24–2.68	1.97–3.12	0.703
SAPS-total score	19.52–12.05	14.51–10.90	0.077
SANS-emotional blunting	11.27–4.27	2.63–2.22	<0.001
SANS-alogia	6.24–2.79	1.25–1.59	<0.001
SANS-apathy	9.12–1.85	5.49–1.36	<0.001
SANS-anhedonia	13.70–3.37	8.97–3.19	<0.001
SANS-attention deficit	6.64–1.59	5.03–1.54	<0.001
SANS-total score	46.97–10.28	23.37–4.99	<0.001
CDSS total score	3.73–2.15	2.49–2.01	0.017
	n (%)	n (%)	
Depression (CDSS cut off for 11)	0 (0)	0 (0)	

SAPS: Positive symptoms evaluation scale, SANS: Negative symptoms evaluation scale
CDSS: Calgary depression scale in schizophrenia

and fT3, high fT4 in schizophrenia (27), and high fT4 in schizophrenia (28). One of these studies was conducted in patients with psychotic exacerbations (27), one in patients who did not have a psychotic exacerbation for one year (11) and the other in patients who had a first episode (26). Other studies did not specify whether patients were in a psychotic exacerbation. Our study consisted of patients without psychotic exacerbation for at least 3 months. Obtaining different results in the studies may have depended on whether the patients were in a psychotic exacerbation period or not. Moreover these differences could be due to the ratio of men and women in the samples, use of psychotropic drugs, history of seizures and obesity (29).

In our study, TSH, fT3, and fT4 levels were not associated with negative, positive, or depressive symptoms. A previous study found no association between TSH level and positive symptoms, however, a negative association was found between negative symptoms (30). In contrast to this study, another study found a positive correlation between TSH levels and negative symptoms (28). This variability in the results, including our study, could be due to the different duration of the disease and the degree of remission of disease symptoms in the patient groups.

The results of our study show that DS patients are not employed at all, whereas the employment rate in the NDS group is very low. This finding indicates that employment and occupational functioning are more impaired when primary deficiency symptoms occur and persist and develop into a deficit syndrome, consistent with previous studies (31,32). As emphasized in previous studies, this can lead to withdrawal from social life, inability to achieve professionally, lower self-esteem, and increased psychopathological symptoms (33).

In our study, no significant difference was found between DS and NDS in suicide attempts, but there was a significant rate of suicide attempts in both groups. Previous studies found that DS was associated with a low risk of suicide, and suicide attempts were more common in NDS (34,35). Delusions are associated with more suicidality in patients with schizophrenia (36). The fact that our patients continue to attend CMHC regularly and receive regular treatment so that positive symptoms subside may explain the lack of difference in suicide rates between the DS and NDS groups in our study. Nonetheless, the presence of high suicide rates in both groups requires the continuation of regular

Table 3. Thyroid hormone levels of the groups

	fT3 (ng/L)	fT4 (ng/dL)	TSH (mIU/L
Normal range	2.3-4.2	0.89-1.76	0.35-5.5
Deficit	3.46–0.56	1.17–0.17	1.67–0.99
Nondeficit	3.43–0.6	1.27–0.37	1.87–1.32
Healthy control	3.17–0.67	1.20–0.33	1.95–1.08
P	0.093	0.398	0.647
	Abnormal fT3, n (%)	Abnormal fT4, n (%)	Abnormal TSH, n (%)
Deficit	3 (9,1)	1 (3)	1 (3)
Nondeficit	3 (8,6)	1 (2.9)	3 (8.6)
Scizophrenia	6 (8,8)	2 (2.9)	4 (5.9)
Healthy control	0 (0)	0 (0)	0 (0)

fT3: free T3, fT4: free T4, TSH: Thyroid stimulating hormone

Table 4. Relationship between thyroid hormone levels and symptoms

		TSH	fT3	fT4	SANS total score	CDSS
fT3	r	-0.033				
	P	0.743				
fT4	r	-0.028	-0.081			
	P	0.776	0.416			
SANS total score	r	-0.092	-0.023	-0.222		
	P	0.455	0.852	0.069		
CDSS	r	-0.095	0.016	0.027	0.267*	
	p	0.439	0.899	0.825	0.028	
SAPS total score	r	-0.063	-0.144	0.048	0.284*	0.498**
	P	0.608	0.242	0.695	0.019	<0,001

fT3: free T3, fT4: free T4, TSH: Thyroid stimulating hormone, SAPS: Positive symptoms evaluation scale, SANS: Negative symptoms evaluation scale CDSS: Calgary depression scale in schizophrenia, *Correlation is significant at the 0.01 level (2-tailed), ** Correlation is significant at the 0.01 level (2-tailed).

treatment.

The limitations of our study can be accepted since it was a single-center study, cross-sectional, there was no long-term follow-up, and psychotropic treatment was continued. In addition, patients diagnosed with mental retardation were not included in the study. Since the participants were followed-up patients from the clinic, additional IQ tests were not applied to the patients.

Consequently, there was no difference in thyroid functions of DS patients compared with NDS and healthy controls. There was no association between positive, negative and depressive symptoms and TSH, fT3, fT4. In future studies, it may be useful to conduct longitudinal studies with larger samples that also consider variables such as psychotic exacerbation period, remission period, and disease duration.

Funding: This research did not receive any specific grants from funding agencies in the public, commercial, or not-for-profit sectors

Conflict of interest: There is no conflict of interest regarding the publication of this article.

Acknowledgement: None

Correspondence address: Assist. Prof. Ali Inaltekin, Kastamonu Unıversity School Of Medicine, Department of Psychiatry, Kastamonu, Turkey ali.inaltekin@hotmail.com

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