The Emotional States and Health-Related Quality of Life in Patients with Thyroid Dysfunction: A Cross-Sectional Study

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Abstract

Background

The potential association between thyroid dysfunction, common psychological problems (depression, anxiety, and stress), and health-related quality of life (HRQoL) have been previously discussed in the literature. The present study aimed to investigate this relationship among the Iranian adult population.

Methods

Participants were 212 patients recruited to the current study from two referral endocrinology clinics in Tehran, Iran, and categorized into hypofunctional (subclinical and overt hypothyroidism), hyperfunctional (subclinical and overt hyperthyroidism), and euthyroid groups. We assessed the emotional states and HRQoL using the 21-item Depression, Anxiety, and Stress Scale (DASS-21) and the Short-Form 12-point Health Survey Version 2 (SF-12v2). Data analysis was conducted using the SPSS version 22.

Results

the current results indicated that those with thyroid dysfunction, both hypofunctional and hyperfunctional groups had significantly higher levels of depression, anxiety, and stress symptoms ($p < 0.05$) as well as poorer HRQoL than their euthyroid counterparts. However, more detailed analysis showed that in participants with hyper- and hypo-functional dysfunction, physical and mental domains of HRQoL were mainly affected, respectively.

Conclusion

Our results showed that thyroid dysfunction could lead to negative emotional states in an adult population. Similar results have been observed regarding HRQoL. Further studies with larger sample sizes considering the subclinical and overt disorders are suggested for future research.

Background

As one of the most prevalent endocrine disorders, thyroid gland dysfunction can cause several disorders such as weight gain or weight loss, probability of infertility and hair loss. In general, thyroid dysfunction can be divided into two groups of hypo- and hyper-thyroidism (1). According to the evidence, the prevalence of hypothyroidism in the Northern Europe, Japan, and the USA is estimated to be in the range of 0.6–12 and 1.3–4 per 1000 individuals for women and men, respectively (2). The Wickham survey has reported a prevalence of 8% for subclinical hypothyroidism in women and 3% prevalence in men. This prevalence can even reach 10% in women older than 55 years (3). For hyperthyroidism, it seems to be a little lower. The NHANES III study has reported a prevalence of 1.3% for this disorder, involving 0.5% for

overt hyperthyroidism and 0.7% for the subclinical disorder. Having a prevalence of 0.5%-2%. Hyperthyroidism affects women ten times more than men (4).

The prevalence of thyroidal dysfunction in Iran has also been investigated. The Tehran Thyroid Study (TTS) investigated thyroidal dysfunction's incidence and prevalence for six years in an Iranian population and reported an annual incidence of 7.62 and 2.0 per 1000 individuals for subclinical and overt hypothyroidism, respectively. However, the incidences were reported to be 0.92 and 0.68 per 1000 individuals for subclinical and overt hyperthyroidism, respectively (5). It is worth noting that hypothyroidism is more common in populations with iodine deficiency, with a prevalence of about 1%-2%, while older women are ten times more likely to be affected than men (6).

Beyond physical complications, there is a potential relationship between thyroid dysfunction, mental health factors, and emotional states (7–10). Many physiological and mental pathways affect individuals' emotional states, commonly characterized by depression, anxiety, and stress, which vary between communities and genders. Mental health disorders are rising globally as well as locally here in Iran. A study in 2015 reported mental disorders prevalence of 23.4% in the general Iranian population, more specifically, 27.6% in women and 19.3% in men (11). Ample evidence has shown irreversible brain impairments due to thyroid hormone deficiency. Moreover, thyroid dysfunction is believed to be associated with mood disorders (4, 12).

In addition, more evidence emphasized the association between thyroid dysfunction and health-related quality of life (HRQoL). HRQoL is an extensive and multidimensional concept subjectively evaluating a given individual's physical, psychological, and social health status. It is influenced by the person's understanding, experiences, and expectations (13). There are minimal studies on the association of thyroidal dysfunction and emotional states and Health-Related Quality of Life (HRQoL). Proper thyroid function likely plays a significant role in emotional stabilization; therefore, thyroid dysfunction may negatively impact the HRQoL, which several factors affect. However, studying the depression, anxiety, stress symptoms, and HRQoL should be conducted considering the culture and background of the societies, mainly if a given study investigates the Iranian population with their considerable religious beliefs and specific traditions and customs. The present study aimed to examine the relationship of thyroidal dysfunction with specific emotional states and HRQoL in a sample of euthyroid individuals, patients with thyroidal hypo- and hyper-functions.

Materials And Methods

The study population included the patients presented to the endocrinology clinic of Taleghani hospital and Loghman Hakim hospital, which are academic hospitals under the Shahid Beheshti University of Medical Science (SBMU), Tehran, Iran, from October 2020 to February 2021. At first, we recruited 383 patients. However, four were excluded later due to their refusal to participate in the study. Eventually, a total of 212 patients who met the inclusion and exclusion criteria were included in the study (Figure 1). The patients were divided into three groups regarding thyroidal function: hypofunctional, hyperfunctional

and euthyroid groups. The euthyroid group included the individuals with normal thyroid function, the hypofunctional group included those with overt or subclinical hypothyroidism, and the hyperfunctional group included the patients with overt or subclinical hyperthyroidism. The study was approved by the Ethics Committee of the SBMU with the ethical approval code of IR.SBMU.ENDOCRINE.REC.1399.118.

The inclusion criteria included the patients of any gender who presented to the related endocrinology clinic with the results of their Thyroid Function Tests (TFT) performed within the last ten days. The test results should have included at least the Thyroid-Stimulating Hormone (TSH) and Free Thyroxine (FT4) levels. Moreover, the patients with prior thyroidal problems, either overt or subclinical, should have received insufficient or no treatment for their disorder at the time of the study. The euthyroid individuals should not have received any thyroid-related treatment as well.

The exclusion criteria excluded any patients with known psychological disorders or those under current treatment for any psychological disorder; patients with any underlying chronic medical condition, such as diabetes, seizure, chronic kidney disease, chronic hepatic disease, malignancy, autoimmune disorder, cardiovascular disease, chronic pulmonary disease, thalassemia, and Acquired Immunodeficiency Syndrome (AIDS); pregnant women; and individuals with recent stressful life events, such as any history of abortion, first-degree relative loss, hospitalization, and divorce within the last six months; as these life events could significantly impact the emotional states and HRQoL.

Definitions of Terms

The hypofunctional group included individuals with subclinical and overt hypothyroidism. Overt hypothyroidism was defined as the concomitant presence of increased TSH and decreased FT4 levels, while subclinical hypothyroidism was defined as increased TSH and normal FT4 levels (14).

The hypofunctional group included individuals with subclinical and overt hyperthyroidism. Overt hyperthyroidism was defined as the concomitant presence of decreased TSH and increased FT4 levels, while subclinical hyperthyroidism was defined as decreased (or even undetectable) TSH and normal FT4 levels (15).

Depression symptoms manifest themselves with a loss of interest or pleasure, sadness, a feeling of guilt or low self-worth, sleep or appetite disturbances, extreme tiredness, and poor concentration (16).

Anxiety is a body's response to a perceived threat and can be triggered by several beliefs, feelings, and thoughts. It manifests itself with worrying thoughts, tension, sweating, swallowing difficulty, dizziness, chest pain, increased blood pressure, respiratory rate, and pulse rate (17).

Stress is a feeling initiated when the individual perceives that demands exceed the resources mobilized by the individual (18).

Research instruments

The study tools included a researcher-made demographic questionnaire, the 21-item Depression, Anxiety and Stress Scale (DASS-21) for emotional states assessment, and the Short-Form 12-point Health Survey Version 2 (SF-12v2) for HRQoL evaluation. All the participants were asked to fill the questionnaires.

Demographic Questionnaire: The participants filled a questionnaire, including the items of age, gender, marital status, residence location, smoking status, physical activity level, and educational level.

21-Item Depression, Anxiety, and Stress Scale (DASS-21): The present study used the Iranian version of the DASS-21, which is the short form of the Depression, Anxiety, and Stress Scale (DASS). The validity and reliability of this version in the Iranian population were investigated and were reported to be satisfactory (19, 20). The questionnaire investigates how frequently a responder feels the emotional states of depression, anxiety, and stress over the past week and includes three subscales with seven items in each subscale. The items are scored based on a 4-point scale from 0 (did not apply to the responder at all) to 4 (applied to the responder very much or most of the time). The total score for each subscale is obtained by summing up the scores of all the related items and then multiplying it by 2. The normal ranges are 0-9, 0-7, and 0-14 for depression, anxiety, and stress, respectively, while scores out of these ranges are considered abnormal. Higher scores indicate a higher frequency of the aforementioned emotional state (21).

Short-Form 12-point Health Survey Version 2 (SF-12v2): Among all the questionnaires assessing the HRQoL, the Short-Form 12-point Health Survey (SF-12v2) has the highest validity and reliability scores (22). This scale assesses the HRQoL within the past four weeks. The present study used the Iranian version of the SF-12v2, whose construct validity and internal consistency had been investigated in the Iranian population and had been reported to be acceptable (23). The questionnaire includes 12 items in 8 subscales as follows: Physical Functioning (PF), Role-Physical (RP), Bodily Pain (BP), General Health (GH), Vitality (VT), Social Functioning (SF), Role-Emotional (RE), Perceived Mental Health (MH).

The first four subscales consist of the Physical Component Summary (PCS), while the second four consist of the Mental Component Summary (MCS). The items are scored based on 2, 3, 5, or 6-point scales, so the score range is different for each item, ranging from 1-2 to 1-6.

The raw scores from the questionnaire need to be modified and transformed. Each of the eight subscales will have a score range of 0-100, with higher scores indicating better health status (24). The Quality Metric Health Outcomes Scoring Software 2 can be used for this purpose. This software can calculate the scores for each item and standardize the PCS and the MCS scores (25).

Statistical Analysis

The continuous variables were described using the mean and standard deviation (mean $\pm$ SD), while the categorical ones were described using the frequency percentage (%). Moreover, the one-way Analysis of Variance (ANOVA) and the Chi-square tests were used for inter-group comparisons of the continuous and categorical variables, respectively. Also, the Analysis of Covariance (ANCOVA) was used to investigate the

correlation of DASS-21 and SF-12v2 scores with the thyroid function while adjusting the age, gender, marital status, educational level, smoking, and physical activity into the model. All analyses were performed using the SPSS version 22 (Chicago, IL, USA) with a significance threshold of p -value=0.05.

Results

A total of 212 participants were enrolled in the present study, including 40(18,9%) men and 172 (81,1%) women. The participants' mean age was 38.17($\pm$ 12.61). The study groups included the hypofunctional group (n = 78), the hyperfunctional group (n = 61), and the euthyroid group (n = 73). The participants' demographics by the group are presented in Table 1. 144 (67.9%) participants were married, while 57 (26.9%) were single. Moreover, 101(47.6%) had a Bachelor's degree or higher educational levels. Also, 17 (8%) of the participants were smokers. No significant inter-group difference was found in age, gender, marital status, educational level, smoking status, and residence location (p > 0.05). However, the euthyroid group had a significantly higher level of physical activity than the two other groups (p = 0.01) (Table 1).

Table 1
Demographic of study participants

	Total n = 212	Euthyroid n = 73	Thyroid hypofunction n = 78	Thyroid hyperfunction n = 61	P- value
Gender					0.399
Male	40 (18.9)	16 (21.9)	11 (14.1)	13 (21.3)	
Female	172(81.1)	57(78.1)	67(85.9)	48(78.7)	
Age	38.17 ± 12.61	36.94 ± 12.67	39.33 ± 12.53	38.13 ± 12.73	0.513
Marital status					0.198
Single	57(26.9)	14(19.2)	23(29.5)	20(32.8)	
Married	144(67.9)	55(75.3)	53(67.9)	36(59.0)	
Divorced/ Widow	11(5.2)	4(5.5)	2(2.6)	5(8.2)	
Education					0.112
Uneducated/primary	43(20.3)	20(27.4)	9(11.5)	14(23.0)	
High school diploma	68(32.1)	19(26.0)	27(34.6)	22(36.1)	
Bachelor/ master or higher	101(47.6)	34(46.6)	42(53.8)	25(41.0)	
Smoking					0.205
Yes	17 (8.0)	5 (6.8)	4 (5.1)	8 (13.1)	
No	195(92.0)	68(93.2)	74(94.9)	53(86.9)	
Physical activity					0.015
High	95 (44.8)	39 (53.4)	38 (48.7)	18 (29.5)	
Low	117(55.2)	34(46.6)	40(52.3)	43(70.5)	
Location					0.583
Tehran	158(76.0)	55(76.4)	55(72.4)	48(80.0)	
Others	50(24.0)	17(23.6)	21(27.6)	12(20.0)	

According to the DASS-21 results, the groups with thyroidal dysfunction had significantly higher scores in all three subscales compared to the euthyroid group ($p < 0.05$). However, the hyperfunctional group had higher scores in depression and anxiety subscales than the hypofunctional group and lower scores in the

stress subscale. The mean values of each DASS-21 subscale and the mean score differences between the dysfunctional groups and the euthyroid group are presented in Fig. 2 and Table 2.

Table 2
The association of Dass21 scores and thyroid status analysis of covariance approach

	Thyroid hypofunction		Thyroid hyperfunction	
	$\beta^{\dagger}$ (95%CI)	p-value	β (95%CI)	p-value
Depression	4.45 (1.00,7.90)	0.012	3.89 (0.27,7.51)	0.035
Anxiety	3.73 (0.55,6.91)	0.022	4.43 (1.07,7.78)	0.010
Stress	5.52 (1.87,9.17)	0.003	5.08 (1.23,8.93)	0.010
$\dagger\beta$ is difference of mean score in each group compared to euthyroid group. CI is confidence interval.				
Participants' age, gender, marital status, education level, smoking and physical activity are adjusted in the model.				

Regarding the HRQoL, both dysfunctional groups had lower scores in all the SF-12v2 subscales than the euthyroid group, except the SF subscale showed an insignificantly higher score in the hyperfunctional group. However, only some of these differences were statistically significant.

According to our findings, the subscales of PF, RP, GH, VT, RE, and MH had significantly lower scores in the hyperfunctional group compared to the euthyroid group (all $p < 0.05$), while there were no significant differences in BP, SF, PCS, and MCS between these two groups (all $p > 0.05$). Regarding the hypofunctional group, the subscales of RE and MH, as well as MCS, had significantly decreased scores compared to the euthyroid group (all $p < 0.05$). However, no significant difference was found in PF, RP, BP, GH, VT, SF, and PCS subscales between these two groups (all $p > 0.05$).

In general, it was evident that the euthyroid patients had a better HRQoL. Regarding the groups with thyroid dysfunction, the hyperfunctional group had decreased scores in most subscales, especially the physical component, while the hypofunctional group had more problems in the mental component (Fig. 3). The SF-12v2 results are presented in Table 3 by groups.

Table 3
The association of SF-12 scores and thyroid status: analysis of covariance approach

	Thyroid hypofunction		Thyroid hyperfunction	
	$\beta^{\dagger}$ (95%CI)	p-value	β (95%CI)	p-value
SF-12				
-Physical Function	-8.25(-19.67, -3.16)	0.190	-14.64(-26.77, -2.51)	0.014
-Role Physical	-9.56(-19.60, -0.47)	0.064	-15.04(-25.66, -4.41)	0.003
-Bodily pain	-2.43(-12.42,7.55)	0.810	-0.44(-11.12,10.23)	0.993
-General Health	-6.88(-16.36,2.59)	0.187	-12.13(-22.23, -2.02)	0.015
PCS	-1.35(-4.93,2.23)	0.611	-3.39(-7.18,0.39)	0.086
-Vitality	-6.06(-15.83,3.69)	0.284	-12.27(-22.67, -1.88)	0.017
-Social Function	-2.63(-13.80,8.53)	0.820	3.42(-8.51,15.35)	0.748
-Role Emotional	-12.81(-23.29, -2.33)	0.013	-16.22(-27.30, -5.13)	0.002
-Mental Health	-12.76(-21.19, -4.32)	0.001	-9.01(-17.98, -0.3)	0.048
MCS	-5.37(-9.69, -1.04)	0.011	-4.34(-8.91,0.23)	0.065
$\dagger\beta$ is difference of mean SF-12 score in each group compared to euthyroid group. CI is confidence interval.				
Participants' age, gender, marital status, education level, smoking and physical activity are adjusted in the model.				

Discussion

According to our results and based on the DASS-21 questionnaire, depression, anxiety, and stress symptoms were more frequently experienced by the patients with thyroid dysfunction than the euthyroid ones. Regarding the SF-12V2 results, patients with thyroid dysfunction had lower levels of HRQoL than euthyroid individuals. These problems were primarily physical in those with subclinical and overt hyperthyroidism, while the patients with subclinical and overt hypothyroidism were mostly affected mentally.

Bathla et al. (2016) investigated the prevalence of depression- and anxiety-related symptoms in patients with hypothyroidism, reporting a significantly higher prevalence of these mental symptoms in these patients (26). Another study by Rakhshan et al. (2016) in Iran compared the mental health between the patients with hypothyroidism and euthyroid individuals and reported that the hypothyroid patients had significantly worse mental health, including all the related components such as depression and anxiety (7). The findings of these two studies were compatible with ours regarding overt hypothyroidism.

However, in addition to patients with overt hypothyroidism, the present study investigated the prevalence of anxiety and depression in patients with subclinical hypothyroidism as well, reporting similar results.

Regarding the negative emotional states in hyperthyroidism, Branka et al. (2015) investigated the physical and mental symptoms in patients with Graves' disease and those with Toxic Nodular Goiter (TNG) before and after surgical intervention. They found that most symptoms, including anxiety and depression, improved significantly with such intervention (27). It is proven that normal brain functioning is affected by thyroid hormones (28). The differences in emotional states symptoms can be attributed to thyroid dysfunctions. The findings of the recent study were compatible with ours in the effect of hyperthyroidism on depression and anxiety. However, the mentioned study showed the impact of an intervention on reducing depression and anxiety in hyperthyroid patients, while we investigated the prevalence of these symptoms in these patients. Moreover, we included those with subclinical hyperthyroidism as well. In a study by Kalra (2011) plenty of stress-induced factors were addressed in patients with hypothyroidism. For instance, the probability of infertility or the increase of health-related expenses (29). Stress is associated with Graves' disease and Hashimoto's thyroiditis as well (30, 31). A survey on primary hypothyroid patients shows that abnormal stress scores were observed at the initial assessment, which is in line with our results (32).

Rakhshan et al. (2016) in Iran also investigated the quality of life in patients with hypothyroidism, reporting lower scores for total quality of life in these patients (7), especially its mental health component. These findings were compatible with ours on lower quality of life in patients with hypothyroidism, especially the mental component of quality of life. However, we included the patients with subclinical hypothyroidism and found similar results as well. Moreover, Branka et al. (2015) investigated the quality of life in patients with hyperthyroidism and reported the improved quality of life in these patients with surgical intervention (27), which was compatible with our findings. However, the mentioned study investigated the effect of an intervention on improving the quality of life in these patients while investigating the prevalence of these symptoms. Moreover, we included those with subclinical hyperthyroidism as well.

Contrary to our findings, some studies reported the lack of any effect on the quality of life due to thyroidal dysfunction, especially in subclinical disorders. For example, a meta-analysis by Feller et al. (2018), including 21 randomized controlled trials and 2192 patients, investigated the effect of medical treatment on symptom improvement and quality of life in patients with subclinical hypothyroidism, reporting no significant effect on both symptom improvement and quality of life (9), which is incompatible with our results on the effect of subclinical hypothyroidism on the quality of life. However, the mentioned study investigated the effect of an intervention on the quality of life, while we investigated the differences in the quality of life between these patients and the euthyroid ones. Moreover, we investigated the patients with overt and subclinical hypothyroidism in a single group together, which could lead to the possibility of a bias. Moreover, a study by Han et al. (2020) on a Korean population found that patients with overt hypothyroidism had improved HRQoL compared to euthyroid individuals. However, this was not true for those with subclinical hyperthyroidism and hypothyroidism (33). These findings are not in line with our

results. These differences can be explained by the small sample size of the overt hypothyroid patients in the mentioned study. The study included only 10 patients with overt hypothyroidism and the rest 987 participants were euthyroid individuals. Another reason can be the differences between quality-of-life assessment tools which were used in both studies.

The present study had multiple strengths. First, we tried to minimize the effect of confounding factors on emotional states, such as stressful life events and chronic diseases, as well as the effect of demographics. Moreover, we investigated the patients with subclinical and overt hyperthyroidism, which few studies have performed to this date. Eventually, we were the first to use the tools of DASS-21 and SF-12v2 for this specific objective in the Iranian adult population. However, the present study had some limitations as well. First, we investigated the patients with subclinical and overt disorders in a single group, affecting the results, leading to a bias. We aimed to analyze each subclinical and overt group separately, but the sample size was relatively small, and the euthyroid individuals were selected from the patients presenting to an endocrinology clinic. Therefore, the findings may not be generalizable to the general population. Eventually, we did not investigate the patients' past medical history and medication history. Consequently, we might have missed the effect of insufficient treatment on groups with thyroid dysfunctions.

Conclusion

According to our findings, we concluded that thyroid dysfunctions can lead to different negative emotional states (depression, anxiety, stress) and decrease HRQoL indicators. It is suggested that patients with thyroid dysfunctions be observed by specialists for their mental health status. It is also recommended to perform further studies with larger sample sizes that consider the subclinical and overt nature of the thyroid dysfunction in the analysis.

List Of Abbreviations

TSH

Thyroid Stimulating Hormone

FT4

Free Thyroxine

HRQoL

Health Related Quality of Life

SF-12V2

Short Form Survey 12 item-Version 2

DASS-21

Depression, Anxiety, Stress Scale- 21 items

PF

Physical Functioning

RP

Role-Physical
BP
Bodily Pain
GH
General Health
VT
Vitality
SF
Social Functioning
RE
Role-Emotional
MH
Perceived Mental Health
PCS
Physical Component Summary
MCS
Mental Component Summary

Declarations

Ethical Approval and Consent to participate:

The study was approved by the Ethics Committee of the SBMU with the ethical approval code of IR.SBMU.ENDOCRINE.REC.1399.118.

Consent for publication:

Not applicable

Availability of supporting data:

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests:

The authors declare that they have no competing interests.

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Authors' contributions:

SMF,AA, PA and FM designed and implemented the studies. SMF,AA and FM were involved in data collection, quality control of the data and data cleaning. AA, PA and FM developed the study concept. SMF, AA designed the study and initiated the collaborative project. LCH performed the statistical analysis, data analysis and interpretation. SMF, AA, PA drafted the manuscript. PA, AA and FM revised the manuscript. All authors reviewed the manuscript and approved the final manuscript. All authors had full access to the data and take full responsibility for the integrity and the accuracy of the data.

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References

1. Yen PM. Physiological and molecular basis of thyroid hormone action. *Physiol Rev.* 2001;81(3):1097–142.
2. Parle JV, Franklyn JA, Cross KW, Jones SC, Sheppard MC. Prevalence and follow-up of abnormal thyrotrophin (TSH) concentrations in the elderly in the United Kingdom. *Clin Endocrinol (Oxf).* 1991;34(1):77–83.
3. Tunbridge WM, Evered DC, Hall R, Appleton D, Brewis M, Clark F, et al. The spectrum of thyroid disease in a community: the Wickham survey. *Clin Endocrinol (Oxf).* 1977;7(6):481–93.
4. Hollowell JG, Staehling NW, Flanders WD, Hannon WH, Gunter EW, Spencer CA, et al. Serum TSH, T(4), and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). *J Clin Endocrinol Metab.* 2002;87(2):489–99.
5. Amouzegar A, Ghaemmaghami Z, Beigy M, Gharibzadeh S, Mehran L, Tohidi M, et al. Natural Course of Euthyroidism and Clues for Early Diagnosis of Thyroid Dysfunction: Tehran Thyroid Study. *Thyroid.* 2017;27(5):616–25.
6. Zimmermann MB. Iodine deficiency. *Endocr Rev.* 2009;30(4):376–408.
7. Rakhshan MP, Ghanbari AB, Rahimi AM, Mostafavi IB. A Comparison between the Quality of Life and Mental Health of Patients with Hypothyroidism and Normal People Referred to Motahari Clinic of Shiraz University of Medical Sciences. *Int J Community Based Nurs Midwifery.* 2017;5(1):30–7.
8. Najafi L, Malek M, Hadian A, Ebrahim Valojerdi A, Khamseh ME, Aghili R. Depressive symptoms in patients with subclinical hypothyroidism—the effect of treatment with levothyroxine: a double-blind randomized clinical trial. *Endocr Res.* 2015;40(3):121–6.
9. Feller M, Snel M, Moutzouri E, Bauer DC, de Montmollin M, Aujesky D, et al. Association of Thyroid Hormone Therapy With Quality of Life and Thyroid-Related Symptoms in Patients With Subclinical Hypothyroidism: A Systematic Review and Meta-analysis. *Jama.* 2018;320(13):1349–59.
10. Leso V, Vetrani I, De Cicco L, Cardelia A, Fontana L, Buonocore G, et al. The Impact of Thyroid Diseases on the Working Life of Patients: A Systematic Review. *Int J Environ Res Public Health.* 2020;17(12).

11. Noorbala AA, Faghihzadeh S, Kamali K, Bagheri Yazdi SA, Hajebi A, Mousavi MT, et al. Mental Health Survey of the Iranian Adult Population in 2015. *Arch Iran Med*. 2017;20(3):128–34.
12. Bégin ME, Langlois MF, Lorrain D, Cunnane SC. Thyroid Function and Cognition during Aging. *Curr Gerontol Geriatr Res*. 2008;2008:474868.
13. Thommasen HV, Berkowitz J, Thommasen AT, Michalos AC. Understanding relationships between diabetes mellitus and health-related quality of life in a rural community. *Rural Remote Health*. 2005;5(3):441.
14. Al Eidan E, Ur Rahman S, Al Qahtani S, Al Farhan AI, Abdulmajeed I. Prevalence of subclinical hypothyroidism in adults visiting primary health-care setting in Riyadh. *J Community Hosp Intern Med Perspect*. 2018;8(1):11–5.
15. Biondi B, Cooper DS. The clinical significance of subclinical thyroid dysfunction. *Endocr Rev*. 2008;29(1):76–131.
16. Marcus M YM, van Ommeren M, Chisholm D, Saxena S. Depression: A global public health concern. WHO, Department of Mental Health and Substance Abuse. 2012.
17. American Psychiatric Association, Diagnostic and statistical manual of mental disorders. 5 ed: 2013; 2013.
18. Ahmad Usman DZA, Ishfaq Ahmed, Zeeshan Akba. Work Stress Experienced by the Teaching Staff of University of the Punjab, Pakistan: Antecedents and Consequences 2011; 2.
19. Asghari A, Saed F, Dibajnia P. Psychometric properties of the Depression Anxiety Stress Scales-21 (DASS-21) in a non-clinical Iranian sample. *International Journal of Psychology (IPA)*. 2029;2(2).
20. Brown TA, Chorpita BF, Korotitsch W, Barlow DH. Psychometric properties of the Depression Anxiety Stress Scales (DASS) in clinical samples. *Behav Res Ther*. 1997;35(1):79–89.
21. Lee D. The convergent, discriminant, and nomological validity of the Depression Anxiety Stress Scales-21 (DASS-21). *J Affect Disord*. 2019;259:136–42.
22. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care*. 1996;34(3):220–33.
23. Montazeri A, Vahdaninia M, Mousavi SJ, Omidvari S. The Iranian version of 12-item Short Form Health Survey (SF-12): factor structure, internal consistency and construct validity. *BMC Public Health*. 2009;9:341.
24. Ware JE, Mark Kosinski, and Susan D. Keller. Sf-12: How to Score the Sf-12 Physical and Mental Health Summary Scales. 2002.
25. Saris-Baglama RN DC, Chisholm GB, Plumb E, Kosinski M, Bjorner JB, Ware JE. QualityMetric Health Outcomes Scoring Software 2.0: User's Guide Lincoln 2007.
26. Bathla M, Singh M, Relan P. Prevalence of anxiety and depressive symptoms among patients with hypothyroidism. *Indian J Endocrinol Metab*. 2016;20(4):468–74.
27. Bukvic B, Zivaljevic V, Sipetic S, Diklic A, Tausanovic K, Stojanovic D, et al. Improved quality of life in hyperthyroidism patients after surgery. *J Surg Res*. 2015;193(2):724–30.

28. Larsen PR, Davies T, Schlumberger MJ, Hay I. Thyroid physiology and diagnostic evaluation of patients with thyroid disorders. Williams Textbook of Endocrinology. 2011:299–332.

29. Kalra S, Verma K, Balhara YPS. Thyro-stress. Indian J Endocrinol Metab. 2017;21(4):632–3.

30. Winsa B, Adami HO, Bergström R, Gamstedt A, Dahlberg PA, Adamson U, et al. Stressful life events and Graves' disease. Lancet. 1991;338(8781):1475–9.

31. Bagnasco M, Bossert I, Pesce G. Stress and Autoimmune Thyroid Diseases. Neuroimmunomodulation. 2006;13(5–6):309–17.

32. Brown BT, Graham PL, Bonello R, Pollard H. A biopsychosocial approach to primary hypothyroidism: treatment and harms data from a randomized controlled trial. Chiropr Man Therap. 2015;23:24.

33. Han M, Choi S, Kim S, Ko A, Son JS, Park SM. Association of Thyroid Status with Health-Related Quality of Life in Korean Older Adults. Korean J Fam Med. 2020;41(1):38–44.

Figures

Figure 1

Flowchart of study participants.

Figure 2

Mean dass-21 questionnaire scores

Figure 3

Mean SF-12 questionnaire scores