

Original Research

Characteristics of thyrotoxicosis among thyroid patients and their quality of life in a teaching hospital in Jordan: A cross-sectional study

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Abstract

Aim: This study aimed to describe the general characteristics of thyrotoxicosis patients, evaluate their quality of life and adherence to medications as an outpatient at endocrine clinic in Jordan. **Method:** This was a descriptive cross-sectional study. The eligible participants, who were patients from endocrine outpatient clinics at JUH were recruited. The inclusion criteria limited the study to patients aged 18 years and older who were newly diagnosed with or had a past diagnosis of hyperthyroidism disease for any cause. Data were analyzed using Statistical Package for Social Sciences version 24.0 (SPSS® Inc., Chicago, IL, USA). **Result:** Most participants were females (81.3%) and married (87.9%). The majority were educated and had a bachelor's degree or higher (41.8%). The average reading for T3 was 6.80 ± 8.26 pmol/l, T4 16.87 ± 7.98 pmol/l, TSH 3.49 ± 11.51 Mu/L, Anti thyroglobulin 2.37 ± 1.73 , and Anti thyroglobulin peroxidase 4.80 ± 1.13 . There were no significant findings in assessing the effect of treatment types on lab tests (p -value > 0.05). The majority of thyrotoxicosis cases were caused by Graves' disease (64.7%), followed by 17.60% from benign multinodular goiter, 11.80% thyroiditis and 5.90% toxic adenoma. There was no significant correlation ($p > 0.05$) between the type of treatments and the following health related quality of life (HRQOL) sub-domains: generally unwell, social problem, muscular skeletal problems, eye problem, classical symptoms of hyperthyroidism (CSH) hand tremor, CSH palpitation, decreased appetite and constipation. **Conclusion:** Thyrotoxicosis is understudied in the Middle East, particularly Jordan. The main findings revealed that thyrotoxicosis is more prominent in females, mainly in their 4th decade. Future work should focus on the main possible methods to improve the HRQOL. In addition, awareness programs are required to encourage patients to obey the advice of their physician and increase their self-care towards improving the quality of their life.

Keywords: Thyrotoxicosis; Quality of life; Adherence; Thyroid medications

INTRODUCTION

The thyroid gland produces two biologically active hormones: free thyroxine (T4) and/or free triiodothyronine (T3). Thyroid hormones are essential for proper fetal growth and development after delivery. The thyroid hormone regulates the body's energy metabolism. Thyroid-stimulating hormone (TSH) is secreted from the pituitary gland and plays an important role in controlling the thyroid axis. It also serves as the most useful physiologic marker of thyroid hormone action.¹ A disturbance in these hormones' levels may lead to significant health disorders.¹

Thyrotoxicosis is a life-threatening state that demands emergency treatment.² It is associated with an excess level of circulating thyroid hormone, which can be T3 or T4 from the thyroid gland and a reduction in the level of TSH released from the pituitary gland. One form of thyrotoxicosis is hyperthyroidism, which occurs due to the thyroid gland's inappropriate high production and secretion of thyroid hormone (TH). Hyperthyroidism is also one of the phases that can arise in a condition called viral thyroiditis, although viral thyroiditis is very rare in children. The hyperthyroid phase of viral thyroiditis usually settles down without treatment.⁴

The incidence rate of hyperthyroidism in men and women from large population studies is 0.4/1000 women and 0.1/1000 men.^{5,6} A meta-analysis to evaluate the incidence rate of thyroid dysfunction reported that the mean incidence rate was 259.12 (254.39-263.9)/100 000 / year: 226.2 (222.26-230.17) and 51 (49.23-52.88) / 100000 / year for hypothyroidism and hyperthyroidism, respectively.⁷

In the United States, the prevalence of hyperthyroidism is 1.2%, subclinical hyperthyroidism accounting for 0.7% and overt hyperthyroidism accounting for 0.5%.⁸ In addition, nationwide surveys were conducted to estimate thyroid storm incidence in Japan. It was assessed to be present in 0.20 persons per 100,000 population per year in Japan, accounting for 5.4% of hospitalized thyrotoxic patients and 0.22% of all thyrotoxic patients.² Another study in Jordan found that the incidence of hyperthyroidism was 2.27% in men and 1.8% in women.

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The undiagnosed prevalence was 2.1% and 1.4% for males and females, respectively. Meanwhile, the incidence of overt hyperthyroidism was 0.3% among males and 0.2% among females.⁹

The therapeutic possibilities available for patients with hyperthyroidism have remained largely unchanged for the past 70 years.¹⁰ The treatment choices for hyperthyroidism are selected based on the cause. It is medically managed via anti-thyroid drugs (ATDs),¹¹ which inhibit thyroid hormone synthesis by blocking iodine oxidation in the thyroid gland.⁸ The best treatment for a specific patient is dependent on the nature and severity of the hyperthyroidism and the patient's age and general health.¹²

Health-related quality of life (HRQOL) has been described as the subjective assessment of the influence of a disease and its treatment, and it is a factor that is self-assessed by the patients via standardized questionnaires.¹³ The importance of HRQOL aspects in evaluating thyroid patients is increasingly recognized in the literature. Numerous features of thyroid diseases have encouraged this increase, especially since the diseases are common and affect men and women of all ages. Moreover, benign thyroid disorders are rarely life-threatening, and therefore their treatment mostly deals with optimizing the patients' quality of life. Additionally, since many thyroid diseases can be treated in several ways, knowledge of the impact of each treatment modality on the HRQOL of the patients is important.¹⁴ Thus, this study aimed to describe the general characteristics of thyrotoxicosis patients, evaluate their quality of life and adherence to medications as an outpatient at an endocrine clinic at Jordan University Hospital(JUH).

METHOD

Study design and participants

This was a descriptive cross-sectional study. The eligible participants, who were patients from endocrine outpatient clinics at JUH, were recruited. The inclusion criteria limited the study to patients aged 18 years and older with newly diagnosed or past diagnoses of hyperthyroidism disease for any cause. Pregnant females were excluded from the study conducted over three months.

Ethical consideration

Ethical approval for the study was obtained from the Faculty

of Pharmacy and the Deanship of Graduate Studies at the University of Jordan. Ethical approval was also obtained from the Institutional Review Board (IRB) of JUH. Written informed consent was provided to patients who agreed to participate in the study after informing them about the nature of the study.

Study instruments

A data collection form was used to collect the following data: patient-related information demographic characteristics, signs and symptoms of thyrotoxicosis, type of treatment (anti-thyroid medication, surgery, radiation), and lab data (TSH, T3, T4, etc..).

The thyroid disease health-related quality of life (HRQOL)

The quality of life for each patient was assessed using the following questionnaire: "Quality of life aspects associated with treated thyroid disease or untreated".¹⁴ This assessment tool consists of five domains, including general aspects, emotional disturbance, symptoms in several thyroid disorders, symptoms of hyperthyroidism, symptoms of hypothyroidism and major complaints (Figure 1).

Self-reported medication adherence questionnaire

The adherence questionnaire was developed and validated by Aburuz et al. based on a scale developed by Morisky et al.¹⁵ The questionnaire was composed of seven questions regarding patients' adherence to their treatment, including how often they forgot to take their medication during the last month, how often they skipped it, and how often they stopped it when feeling better, worse or when they experienced it a side effect. The scale followed in the adherence questionnaire was composed of: never, rarely, sometimes, often, and always.

Sample size

In a study by Ajlouni⁶ to assess hyperthyroidism in Jordan, the average prevalence of the disease was reported to be 15 %.Based on this data, the present sample size was calculated using a margin of error of 5%, a confidence level of 95%, and a response distribution of 50%, giving a minimum sample of 192 patients.

Sample size calculation is shown below:

P =expected proportion in population-based on previous studies or pilot study=15%

d = absolute error or precision – has to be decided by research= 5%

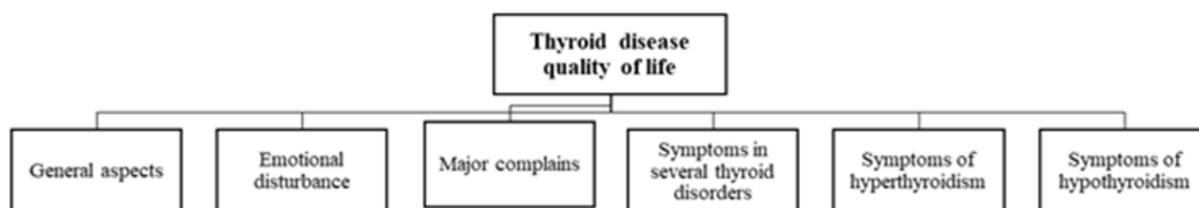


Figure1. Summary related to thyroid disorder quality of life (Torquil Watt1, (2006))



Statistical analysis

Data were analyzed using Statistical Package for Social Sciences version 24.0 (SPSS® Inc., Chicago, IL, USA). The descriptive statistics included percentages, means, and frequency distribution, which were calculated for each question. Descriptive and univariate correlation analyses using Pearson correlation coefficient (r) were used for the correlation, which was conducted at a 5% significance level. Factors affecting health-related quality of life were analyzed via nominal regression. A p-value of < 0.05 represented a significant difference. The normality of the data was checked using the Shapiro–Wilk test.

RESULTS

Sociodemographic characteristics

Due to time constraints, 121 patients were recruited, and among them, only 91 were eligible and included in the study. The majority of participants were female (81.3%), married (87.9%), and educated and had a bachelor’s degree or higher (41.8%). Almost all study participants had health insurance and 12.1% were newly diagnosed with thyrotoxicosis (Table 1). About half of the study participants were treated with surgery (48%), anti-thyroid medications (42%), and radiation (10%) (Figure 2). The family history of the patients was also assessed, and the following was found: one-third of them had a family history of thyroid diseases, hypertension (HTN), and diabetes mellitus (DM) (Figure 3).

Thyroid hormones profile assessment

Thyroid hormones profiles (T3, T4, TSH, Anti thyroglobulin, Anti thyroglobulin peroxidase) were collected (Table 2). The average reading for T3 was 6.80±8.26 pmol/l, T4 16.87±7.98 pmol/l, TSH 3.49±11.51 Mu/L, Anti thyroglobulin 2.37±1.73, and Anti thyroglobulin peroxidase 4.80±1.13. There were no significant findings in assessing the effect of treatment types on lab tests (p-value >0.05).

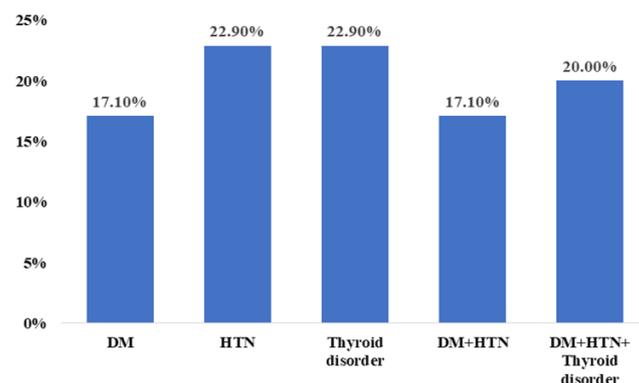


Figure 3. Family history related diseases

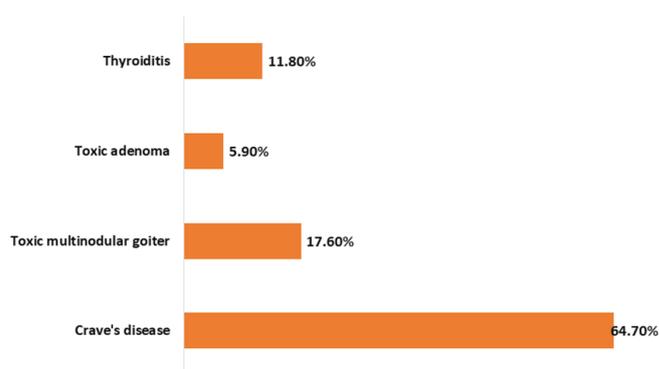


Figure 4. Patient's conditions causing thyrotoxicosis N=91, N (%)

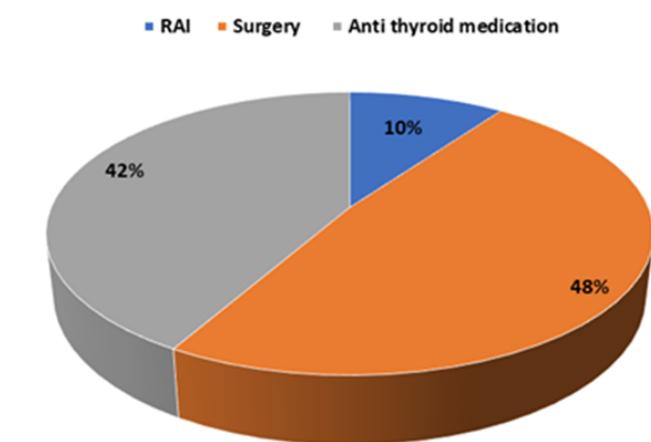


Figure 2. Types of treatment of Thyrotoxicosis

Signs and symptoms of thyrotoxicosis

In assessing signs and symptoms of thyrotoxicosis, between one half and a third of the total number of patients had tremors (28.6%), goiter (33.0%), weight loss (36.3%), nervousness (36.3%), palpitations (41.8%), tiredness (42.9%) and increased sweating (23.1%). The majority of thyrotoxicosis cases were caused by Graves’ disease (64.7%), followed by benign multinodular goiter 17.60%, thyroiditis 11.80% and toxic adenoma 5.90% (Figure 4). Among patients who have Graves’ disease (N=22) or a benign multinodular goiter (N=6), similar patterns of signs and symptoms (Table 3).

Health-related quality of life (HRQL) assessment

Health-related quality of life is composed of six domains (Table 4). Most of the patients (98.9%) felt generally unwell when assessing general aspects. Under the “emotional disturbance” domain, 18.7% had anxiety. Their “major complaints” were fatigue (48.4%), followed by weight problems (19.8%). In the “Symptoms in several thyroid disorder” domain, 12.1% of the patients reported experiencing eye problems and 7.7% reported changes in hair and nails and complained of compression. About 26.4% experienced palpitations as a classical symptom of hyperthyroidism, followed by 15.4 % experiencing increased sweating and 13.2% experiencing hand tremors. The last domain was “symptoms of hypothyroidism,”

Age (years) Mean± SD	48.14±15.90
Gender	
• Male	17(18.7)
• Female	74(81.3)
Marital status	
• Single	11(12.1)
• Married	80(87.9)
Educational level	
• Not educated	9(9.8)
• High school	27(29.7)
• Diploma	17(18.7)
• Bachelor or higher	38(41.8)
Insurance	
• Insured	89 (97.8)
• Not insured	2(2.2)
Newly diagnose with thyrotoxicosis	
• Yes	11(12.1)
• No	80(87.9)

and only 3.3% had constipation and decreased appetite. This type of treatment was found to have a statistically significant (p-value <0.05) effect on the following sub-domains: generally unwell, social problem, muscular skeletal problems, eye problem, classical symptoms of hyperthyroidism (CSH) hand tremor, CSH palpitation, decreased appetite and constipation.

Nominal regression outcomes (Table 5) showed no significant correlation (p>0.05) between the type of treatments and the following HRQOL sub-domains: generally unwell, social problem, muscular skeletal problems, eye problem, CSH hand tremor, CSH palpitation, decreased appetite and constipation.

Self-reported medication adherence questionnaire

More than half of the patients (58.1%) had “never” forgotten to take their medications, while 56.5% had “never” been careless about taking their drugs (Table 6). The majority (72.6%) of them “never” stopped their drugs when they felt better. About 91% of the patients either “never” or “rarely” stopped their medications if they felt worse. Almost two-thirds of them “never” or “rarely” stopped taking their medication if they had

Thyroid hormone profile*	Mean ± SD	Min	Max	P-value**
T3 (pmol/l)	6.80±8.26	2.90	46.08	0.175
T4 (pmol/l)	16.87±7.98	.23	54.70	0.322
TSH (Mu/L)	3.49±11.51	.0005	100.00	0.338
Anti thyroglobulin	2.37±1.73	1.14	3.60	-
Anti thyroglobulin peroxidase	4.80±1.13	4.00	5.61	-

*T3=Triiodo thyroxine, T4=thyroxin, TSH=thyroid stimulating hormone, Min=minimum, Max=maximum, SD=standard deviation, pmol/l= picomole/liter, Mu/L=milliunits per liter; **Pearson Chi-square test

	Total (91)	Graves' disease (22)	Benign multinodular goiter (6)
Tremor	26(28.6)	12(54.5)	4(66.7)
Goiter	30(33.0)	10(45.5)	3(50.0)
Lid lag	2(2.2)	2(9.1)	0(0.0)
Tachycardia	15(16.5)	4(18.2)	1(16.7)
Palpitation	38(41.8)	20(90.9)	3(50.0)
Exophthalmos	12(13.2)	7(31.8)	0(0.0)
Bruit	2(2.2)	1(4.5)	0(0.0)
Hypo pigmentation	3(3.3)	0(0.0)	0(0.0)
Hyper pigmentation	0(0.0)	0(0.0)	0(0.0)
Weight loss	33(36.3)	18(81.8)	3(50.0)
Nervousness	31(34.1)	15(68.2)	4(66.7)
Hypersensitivity to the head	1(1.1)	0(0.0)	0(0.0)
Increased sweating	21(23.1)	7(31.8)	2(33.3)
Increased appetite	8(8.8)	1(4.5)	0(0.0)
Menstrual disturbance	7(7.7)	3(13.6)	1(16.7)
Diarrhea or loss of bowel	3(3.3)	2(9.1)	0(0.0)
Tiredness	39(42.9)	16(72.7)	4(66.7)
Muscle weakness	19(20.9)	7(31.8)	2(33.3)

N=number of patients



Table 4. Health-related quality of life (HRQOL) assessment for patients only N=91

Measure	N (%)	P-value *
General aspects		
• Reduced general health perception	0(0.0)	-
• Generally unwell	90(98.9)	0.010
• Limitation in unusual activities	4(4.4)	0.471
• Social problem	1(1.1)	0.583
Emotional disturbance		
• Emotional lability	2(2.2)	0.888
• Anxiety	17(18.7)	0.552
• Lack of familiar sense of self	3(3.3)	0.383
Major complains		
• Fatigue	44(48.4)	0.132
• Sexual problem	0(0.0)	-
• Cosmetic complaint	4(4.4)	0.535
• Hallucination	5(5.5)	0.330
• Dizziness	12(13.2)	0.824
• Weight problem	18(19.8)	0.014
• Muscular skeletal problems	15(16.5)	0.607
Symptoms in several thyroid disorders		
• Headache	2(2.2)	0.335
• Sleep disturbance	2(1.1)	0.583
• Bowel disturbance	3(3.3)	0.158
• Menstrual disturbance	4(4.4)	0.471
• Eye problem	11(12.1)	0.021
• Compression complaints	7(7.7)	0.541
• Dyspnea	4(4.4)	0.369
• Change hair nail skin	7(7.7)	0.227
• Chest pain	2(2.2)	0.888
Symptoms of hyperthyroidism		
• CSH heat intolerance	8(8.8)	0.812
• CSH hyperactivity	5(5.5)	0.397
• CSH increased appetite	4(4.4)	0.054
• CSH increased sweating	14(15.4)	0.932
• CSH diarrhea	3(3.3)	0.750
• CSH hand tremor	12(13.2)	0.007
• CSH palpitation	24(26.4)	0.002
Symptoms of hypothyroidism		
• Cold intolerance	1(1.1)	0.583
• Diminished sweating	0(0.0)	-
• Change in voice	0(0.0)	-
• Edema	0(0.0)	-
• Decreased appetite	3(3.3)	0.003
• Nausea vomiting	0(0.0)	-
• Constipation	3(3.3)	0.003

• Hearing problem	0(0.0)	-
• Disturbance in the peripheral nervous system	4(4.4)	0.227
• Enlarged tongue	1(1.1)	0.583

N=number of patients, CSH=Classical symptoms of hyperthyroidism *Pearson Chi-square test in correlation with different types of treatment. Significance (p<0.05) presented in bold numbers

Table 5. Summary of the nominal regression analysis to assess HRQOL factors associated with the type of treatments

Independent factors	Nominal regression	
	Beta	P-value
Generally unwell	-26.475	0.993
Social problem	-	-
Weight problem	-0.008	1.000
Eye problem	12.533	0.848
CSH hand tremor	-7.485	0.873
CSH palpitation	-20.220	0.831
Decreased appetite	-23.877	0.982
Constipation	66.633	0.950

Table 6. Assessment of patients' adherence to medications

Questions	N (%)
Do you ever forget to take your prescription Drug?	
• Never	36(58.1)
• Rarely	16(25.8)
• Sometimes	9(14.5)
• Usual	1(1.6)
• Always	0(0.0)
Are you careless at times about taking your drugs?	
• Never	35(56.5)
• Rarely	21(33.9)
• Sometimes	4(6.5)
• Usual	1(1.6)
• Always	1(1.1)
Do you sometimes stop taking your drugs when you feel better?	
• Never	45(72.6)
• Rarely	11(17.7)
• Sometimes	4(6.5)
• Usual	2(3.2)
• Always	0(0.0)
Do you sometimes stop taking your drugs if they make you feel worse?	
• Never	39(62.9)
• Rarely	19(30.6)
• Sometimes	2(3.2)
• Usual	1(1.1)
• Always	1(1.1)
Do you stop taking your drugs if they caused you side effects that resulted from taking them?	
• Never	37(59.7)
• Rarely	19(30.6)
• Sometimes	3(4.8)
• Usual	2(3.2)
• Always	1(1.6)



Are you committed to the advice given by the doctor/ pharmacist concerning exercise, diet, smoking, etc.?	
<ul style="list-style-type: none"> • Never • Rarely • Sometimes • Usual • Always 	<p>21(33.9)</p> <p>34(54.8)</p> <p>7(11.3)</p> <p>0(0.0)</p> <p>0(0.0)</p>
How many times per week you don't take your medications mean±SD	0.661±1.213

experienced side effects. However, the majority (88.7%) were “never” or “rarely” committed to the advice given by their doctors. The average time per week that patients don't take their medications was 0.661±1.213.

DISCUSSION

Thyroid dysfunction is one of the most common diseases around the world.¹⁶ This study was concerned about one particular thyroid dysfunction disease, thyrotoxicosis. This disease has been understudied in the Middle East, particularly in Jordan. The main findings revealed that thyrotoxicosis is more prominent in females who are in their forties. Similar results have been published recently in Italy,¹⁷ where it was reported that the prevalence of hyperthyroidism was two-fold higher among women than men aged between 30-50 years old.¹⁷ On the contrary, a recent Jordanian cross-sectional study stated that the prevalence of diagnosed hyperthyroidism in males was almost 1.5 fold that of females, and the undiagnosed prevalence was 1.4% and 2.1% for females and males, respectively.⁹ However, the results of this study and our study matched the high prevalence of thyroid diseases compared with the global statistics. Accordingly, there is a tremendous need to focus on this category of patients in all terms, including awareness, quality of life and compliance for medications. Although there is a high prevalence of thyroid diseases in the Jordanian studies, the variation in the results between studies may be explained by differences in the level of health-related literacy of the study participants, the number of the population, the economic status of the patients.⁹

One-third of the study's patients had a family history of thyroid diseases and other chronic comorbidities, such as hypertension and diabetes. Such findings were not surprising, as many studies have confirmed a relationship between the incidence of thyroid disorders and multiple factors, including age, gender and family history.^{18,19} In Jordan, a study conducted in 2009 by Ismail et al. reported on the detection of combined genomic variants in families with hyperthyroidism.²⁰

The management of hyperthyroidism usually depends on the cause and severity of the disease and the patient's age, goiter size, co-morbid conditions, and the treatments recommended by physicians.²¹ In this study, the majority of the participants were treated with surgery, followed by anti-thyroid medications and radiation. This is contrary to the preferences of endocrinologists, who nominate the use of anti-thyroid medications, radiation, then thyroidectomy.²² Even with treatment, more than half of the study participants were sub-optimally controlled and complained mostly of tiredness

and goiter. Moreover, the symptoms were more serious with the Graves' disease-thyrotoxicosis patients, who experienced weight loss/palpitations. Published reports have disclosed similar findings, as tremor/goiter (both 90%) were the most common sign, while nervousness (80%) was the most common symptom for hyperthyroidism, as previously reported.⁶ Unsurprisingly, all these findings substantially affected patients' health-related quality of life.

This study documented poor quality of life in terms of health among the participants. Mostly, they were feeling unwell with noticeable emotional disturbances. Such findings have been reported by Bianchi et al., who found that mood/behavior disturbances in a large proportion of thyroid-patients and were significantly associated with poor HRQOL.²³ On the contrary, a Western European study was conducted in 2013 to assess the relationship between the HRQOL and thyroid hormone status. Their study results did not show a significant correlation between high TSH levels and the quality of life.²⁴ Of note, HRQOL is a function of many factors, not only thyroid hormone statuses, such as sociodemographic status, presence of comorbidities and thyroid-related symptoms.^{24,25} Klaver et al., reported that thyroid-related symptoms, such as chronic fatigue, dry hair, chronic irritability, and nervousness, were significantly associated with lower quality of life.²⁴ In Jordan, this is the first study to assess thyroid patients' quality of life, highlighting the sub-optimally managed symptoms and their poor quality of life, despite their admission for medication adherence. There is a pressing need to focus on this category of patients and determine the best methods to improve the HRQOL through future research work.

Study limitation

This study had several limitations, including the sub-optimal study size and limited access to some endocrine clinics (some physicians refuse to participate). The study participants were recruited from a tertiary care/university hospital and as such, the results might not be generalizable to other health care settings.

CONCLUSION

In conclusion, the results of this study reveal that the prevalence of thyroid dysfunction among the adult population of Jordan is very high. Furthermore, this study documented poor quality of life in terms of health among thyroid disease patients, who were sub-optimally controlled with treatment. Hence, there is a need for national recommendations for the management (diagnosis, treatment, and follow-up) of patients with thyroid disorders in order to improve their HRQOL in Jordan. Awareness programs are also required to encourage patients to obey their physician's advice and improve their self-care towards their disorder.

CONFLICTS OF INTEREST

All authors declare that they have no conflicts of interest.

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