Original Research Article

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DEPRESSION AND ADHERENCE TO LEVOTHYROXINE AMONG PATIENTS WITH HYPOTHYROIDISM IN TABUK, SAUDI ARABIA.

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ABSTRACT:

Background: Hypothyroidism is prevalent worldwide, levothyroxine acts at a cellular level leading to a wide range of physical and psychological disorders. Medication adherence is vital for thyroid hormone stimulating hormone normalization and resolution of symptoms. The current study aimed to assess depression and adherence to levothyroxine among patients with hypothyroidism.

Subjects and Methods: This cross-sectional study conducted among 229 participants attending an Endocrine clinic in King Fahd Specialist Hospital from October 2019 to February 2020. A structured questionnaire based on demographic data and the HADS depression scale was used. Participants signed written informed consent, then responded to the questionnaire. The Ethical Committee of the Medical College approved the research. All the participants signed a written informed consent and the Statistical Package for Social Sciences (SPSS) (IBM, version 20, New York was used for data analysis.

Results: There were 229 patients (76% females), their mean age was 33.99±11.25 years, 63% were married. The majority (95.3%) received higher education, and 41.3% were not compliant with their medications. In the current study, 41.6% of patients with hypothyroidism were depressed, with borderline, moderate, and severe depression observed in 30.4%, 27.1%, and 14.5% respectively. Adherence to thyroxine was associated with improvement of depressive symptomatology, P-value <0.05.

Conclusion: Depression and non-adherence to levothyroxine were prevalent among patients with hypothyroidism in Tabuk City, those who were non-adherent to thyroxine therapy showed less improvement in depression symptoms. Further larger multi-center studies assessing barriers to levothyroxine intake are needed.

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INTRODUCTION

Depression is a rapidly growing mental disorder, in the year 2008, the World Health Organization ranked depression as the third cause of disease burden across the globe and expected to jump to the first position by the year 2030 [1], the burden of depression is great and ranging from somatic symptoms to psychosocial pain and suicide [2,3].

Thyroid disease is a global health burden that can substantially affect the patient's well-being, hypothyroidism is not uncommon and may range from 9.1% to 17.2% in men and women respectively [4,]. Overt hypothyroidism may cause symptoms of depression because the brain is a primary target organ for thyroid hormone. However, the symptoms of depression may or may not completely resolve with thyroid replacement therapy (levothyroxine (L-T4)). Also, depressive symptoms are sometimes attributed to subclinical hypothyroidism with overtreatment with thyroxine with attendant risks of osteoporosis and cardiovascular disorders [5].

Depressive symptoms are among the commonest thyroid symptomatology together with other comorbidities including diabetes, hypertension, and anxiety disorders [6]. A recent review and meta-analysis showed an increasing prevalence of depression and anxiety among patients with autoimmune thyroiditis which is the leading cause of primary hypothyroidism worldwide [7]., The earlier detection of depression among patients with primary hypothyroidism has important implication in the form of early introduction of psychotherapy.

A study conducted among 1410 patients in the European for the Study of Persistent Depression found that hypothyroidism is associated with the severity of depression with no influence on treatment response [8]. Some studies suggested a correlation of thyroid-stimulating hormone (TSH) with depression severity with THS of 2.5MIU/L for depression and 4.0MIU/L for severe depression [9]. The literature on the prevalence of depression in the Kingdom of Saudi Arabia is scarce, there is interregional, sex, and age differences with a range between 35% and 55% [10], a study included 477 participants in the primary healthcare setting showed a prevalence of 49.9% (31% were mild, 13.4% moderate, 4.4% moderate-severe and 1.0% severe cases [11].

Levothyroxine is available in the form of oral capsule gel and oral solution in addition to the tablet, the American Thyroid Association and, and the American Association of Clinical Endocrinologists recommend the consistent use of thyroid preparation for the individual patient to avoid variability, the regular and consistent use is of paramount importance to normalize thyroid hormone levels [12,13], a study with a long period of follow-up reported that 22% of hypothyroid patients had a high thyroid-stimulating hormone (TSH) levels due to non-adherence [13]. A letter published in The Lancet calls for more research on levothyroxine adherence [14]. The data on levothyroxine adherence are scarce in the Kingdom of Saudi Arabia. Given the above and the fact that no studies have assessed the prevalence of depression and adherence to thyroid replacement in Tabuk City. The present survey aimed to investigate the prevalence of depression and adherence to thyroxine among patients with hypothyroidism in Tabuk, Saudi Arabia.

MATERIAL AND METHODS

This cross-sectional study conducted among 229 participants attending an Endocrine clinic in King Fahd Specialist Hospital from October 2019 to February

2020. The sample size was calculated using the formula: n=Z2 P-Q/d2 where Z = 95% confidence (1.96), P = Prevalence of hypothyroidism in Saudi Arabia3, Q=100-prevalence, and d=tolerated error. All the adults' patients with the diagnoses of hypothyroidism and who were prescribed thyroxine were included; children and pregnant ladies were excluded. A structured questionnaire was used for data collection, it consisted of two parts, socio-demographic data, including age, sex, marital status, nationality, level of education, occupation, symptoms before and after thyroxine, if on regular follow-up, if adherence to thyroxine, the dose of thyroxine taken, and improvement of symptoms following thyroxine administration. The second part consisted of the HADS questionnaire to assess depression among the participants, the questionnaire consists of seven components, each component with four different shades ranging from zero-3, with three indicating maximal score. A score of 0-7 is regarded as normal, while scores of 8-10, 11-14, and ≥ 15 indicating mild, moderate, and severe depression respectively. The Arabic version of the questionnaire has been previously validated for use in outpatients, emergency, and Hospital settings with good sensitivity and specificity [15].

The Ethical Committee of the Medical College approved the research. All the participants signed a written informed consent and the Statistical Package for Social Sciences (SPSS) (IBM, version 20, New York was used for data analysis.

RESULTS

There were 229 patients (76% females), their mean age was 33.99±11.25 years, 63% were married. The majority (95.3%) received higher education, 19.2% were students, 15.2% were employees, 23.5% were teachers, and 3.8% were soldiers. It is interesting to note that, more than half were not on regular follow-up, 23.8% showed no or mild improvement with thyroxine, and 41.3% were not compliant with their medications. Table 1.

Regarding the symptoms before the institution of thyroxine, 56.1% of the sample study has increased in their weighting before taking medicine.99.5% of the sample study has forgetfulness before taking medicine, while, 19.4%of the sample study have Abundant in the period before taking thyroxin. Table 2.

In the current study, 7.9% of the sample study have hair loss after taking

Table 1. Basic characters of the study group

Character	No %
Age	33.99±11.25
Sex	
Males	55 (24%)
Females	174 (76%)
Marital status	
Married	144 (63%)
Unmarried	65 (28.3%)
Divorce	7 (3.1%)
Others	13 (5.6%)
Nationality	
Saudi	206 (89.9%)
Non-Saudi	23 (10.1%)
Education	
Illiterate	5 (3.5%)
Basic education	19 (8.3%)
Higher education	202 (88.2%)
Occupation n	
Employee	35 (15.2%)
Teacher	54 (23.5%)
Soldier	9 (3.8%)
Not working	107 (46.7%)
Student	24 (10.4%)
Follow-up	
Yes	110 (48%)
No	119 (52%)
Subjective improvement with thyroxine	73 (16.4%)
Mild	68 (15.2%)
Moderate	41 (9.2%)
High	32 (7.2%)
No	
Taking medications	
Yes	136 (59.4%)
No	24 (10.5%)
Sometimes	69 (30.1%)

medicine.29.9% of the sample study to have a problem in breathing after taking medicine.26.6% of the sample study to have Perspiration after taking medicine. Table 3

In the present study, 25.8% of participants were taking only 25micrograms of thyroxine per day, 19.5% were on50 microgram, 11.8% on 75 micrograms, 20.9% on 100 micrograms, 10.9% were on 150 micrograms/day, 2.6% were taking 175microgram, and only a minority were on >175 micrograms/day. Table 4.

In the current study, 72% of patients with hypothyroidism were depressed, with mild, moderate, and severe depression observed in 30.4%, 27.1%, and 14.5% respectively. Table 5.

In the current study, patients who were adherent to thyroxine therapy showed higher improvement in depression symptoms (70.6% vs. 29.4%, P-value=0.04. 95% CI=1.08-3.35. Table 6.

Table 2: Symptoms before treatment

Symptom	No%
Forgetfulness	195 (99.5%)
Dry skin	116 (59.2%)
Increasing weight	110 (56.1%)
Menorrhagia	67 (34.2%)
Infertility	36 (18.4%)
Hearing problem	45 (23.0%)

Table 3: Symptoms after treatment

Symptom	No%
Loss of hair	17 (7.9%)
Shortness of breath	64 (29.9%)
Sweating	57 (26.6%)
Anemia	41 (19.2%)
Palpitations	135 (69.1%)
Hearing problem	45 (23.0%)

Table 4. Thyroxine dose among the study group (no=229)

Character	No %
25 micrograms	59 (25.8%)
50 micrograms	45 (19.5%)
75 microgram	27 (11.8%)
100 micrograms	48 (20.9%)
150 micrograms	25 (10.9%)
175 micrograms	6 (2.6%)
>175 micrograms	4 (1.7%)

Table 5. Depression among patients with hypothyroidism

Depression	No% (total no=214)
Borderline	65 (30.4%)
Moderate	58 (27.1%)
Severe	31 (14.5%)

DISCUSSION

The prevalence of depression varied considerably by location and time, it was found to be 5% in the United States in the year 2018, in 1ndia the prevalence was 12% in the year 2016, and 2% in the United Kingdom. A study published in AL Khobar, the Kingdom of Saudi Arabia found a prevalence of 33.9% of depression among hypothyroid patients and was lower than the current findings in which 41.6% of hypothyroid patients were depressed [16]. The discrepancies between the different studies may be attributed to age, gender, and other sociodemographic features. The method of depression assessment may significantly affect the rate of depression. A study conducted in India and used the Hamilton Depression Rating Scale found that 60% of hypothyroid patients reported some degree of depression similar to the current observation [17]. In the current study, 40.1% of patients with hypothyroidism were not adherent to thyroxine treatment in line with a previous study [18] that showed 40.3% of patients were not taking thyroxine regularly after six months of treatment initiation. Another

Table 6. Effects of medication adherence on depressive symptoms among the study group

Character	Adherent	Non-adherent	P-value	95% *CI*
Improvement of depression symptoms	77 (70.6%)	32 (29.4%)	0.024	1.08-3.35

*Chi-square test

study found that 48.7% were not adherent in accordance with the present data [19], non-adherence to thyroxine is mirrored by the findings that nearly a half of the sample showed no improvement of their symptoms while on thyroxine replacement. In the current study, forgetfulness and dry skin were the most common presentations in line with the previous literature; it is interesting to note that the majority of patients with hypothyroidism were on thyroxine dose ranging from 25-100 microgram in line with Mohammed and Colleagues from Saudi Arabia [16]. In the current survey, patients who were adherent to thyroxine therapy showed higher improvement in depressive symptomatology compared to their counterparts with significant statistical difference in line with a study published in the USA [20], similar results were shown by Li et al. in China [21].

The study limitations were the reliance on a self-administered questionnaire which is more prone to subjectivity and the fact that the study was conducted at a single-center, so generalization to the whole Kingdom cannot be insured.

CONCLUSION

Depression and non-adherence to levothyroxine were prevalent among patients with hypothyroidism in Tabuk City, those who were adherent to thyroxine showed higher improvement in depression symptoms, measures to improve compliance and the earlier detection and treatment of depression are needed.

Conflicts of interest: none to declare

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