

Prevalence and Associated Factors of Depressive Symptoms among Adults with Overt Hypothyroidism on Treatment in Riyadh: A Cross-Sectional Study

Dalal Marji Alruwaili^{1*} and Fayeze Alanazi²

¹Department of Family Medicine, Prince Mohammed Bin Abdul-Aziz Hospital, Riyadh, Saudi Arabia

²Consultant Family Medicine in Prince Mohammed Bin Abdulaziz Hospital -Riyadh -Saudi Arabia

*Corresponding author

Dalal Marji, Department of Family Medicine, Prince Mohammed Bin Abdul-Aziz Hospital, Riyadh, Saudi Arabia, Tel: +966535495457; E-mail: alruwailidalal9@gmail.com

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Abstract

Background: There is strong association between depression and hypothyroidism. People with a chronic disease and on lifelong medication are more likely to have poorer mental health than those with no illnesses. This study aimed to measure the prevalence and associated factors of depressive symptoms in adults with overt hypothyroidism on treatment in primary care clinics in Riyadh.

Methods and findings: Cross-sectional study of 369 patients with overt hypothyroidism visiting primary care clinics and endocrine outpatient clinics at Prince Mohammed bin Abdul-Aziz hospital. Data were collected using an Arabic validated version of the Patient Health Questionnaire-9 for screening of depression among the participants. Prevalence of depression among adult patients with hypothyroidism on treatment was 56.1%. It was moderately severe and severe among 58.7% and 33.3% of depressed patients.

Conclusions: Depression is a common health problem among patients with overt hypothyroidism on thyroxin treatment, majority of patients has moderately severe to severe depression. Depression was more observed among older (≥ 40 years), female, divorced/widowed and lower educated patients compared to their counterparts. Also, it was more reported among patients with longer duration of hypothyroidism. No association was observed with levels of TSH and thyroxin hormones.

Introduction

Background and Literature Review

Hypothyroidism is diagnosed when there is a decrease in the production of thyroid hormone with an increased level of thyroid stimulating hormone (TSH). It has recently increased and is considered one of the most common endocrine diseases [1]. The causes can be classified into primary ones that are dysfunction in the thyroid gland itself and secondary causes related to a defect in the pituitary or hypothalamus [2]. The thyroid gland secretes three hormones: thyroxine (T4), triiodothyronine (T3) and calcitonin. T4 and T3 are necessary for normal brain development and function; it has a greater effect on metabolism [3]. Oral Thyroxine is used in the treatment of hypothyroidism and dose varies from patient to patient [3].

Hypothyroidism has a significant impact on physical and mental health [4,5]. One of the most psychiatric disorders associated with hypothyroidism is depression [6].

Depression is a mental illness, which is considered by the World Health Organization to be the second largest killer disease after heart disease by 2020 [7,8]. Many studies show that there is a

significant relationship between hypothyroidism and depression, there is an overlap between their symptoms such as loss of interest, lethargy, loss of appetite, sleeping too much, poor memory, loss of concentration and decreased libido. These psychological symptoms can severely affect quality of life [3,7,9].

Many researchers have revealed that there is a significant link between hypothyroidism and depressive symptoms. In Brazil, they studied the association between hypothyroidism and depressive symptoms among middle age women, the prevalence of depression was reported at about 45.7% and 12.3% were presented with hypothyroidism [10]. In Spain, the overall prevalence of hypothyroidism in major Psychiatric Disorders was 10.5%, 11.1% was in depressive disorder [11].

In Delhi (2013) it was revealed that the prevalence of hypothyroidism in depressed patients was 20% and depression in hypothyroidism was 36.67% [6]. In India, the prevalence of depressive symptoms in hypothyroidism has been reported to be 60% [4]. In Nepal, 21% of patients with depression had thyroid dysfunction [12].

In Italy (2012) it has shown that the overall prevalence of depressive

symptoms in the population with subclinical hypothyroidism was 63.5% however, treatment with levothyroxine alone was not sufficient to induce complete remission of symptoms of depression in this population. In patients treated with T4, psychological symptoms may persist even when the euthyroid state is achieved [13]. In several studies, no association could be found between severity of depression and TSH levels [14].

In UK, they found a clear association between higher TSH and lower free T4 and poorer psychological well-being in 697 subjects on thyroxin. The prevalence of depression in females on thyroxin was higher than that in females not on thyroxin [15,16].

In Riyadh, Saudi Arabia (2018) the incidence of hypothyroidism in adult female was 15.5% [1]. Also in Riyadh, Al Eidan E, et al reported 49.9% as a prevalence of depressive symptoms in adult visiting primary care [17]. In Albahah city, the prevalence of hypothyroidism was 42.8% in female and 25% in male according to a study carried out by Gaffer Ali AA and Altahir SA [18].

Research Objectives

- This study aimed to measure the prevalence of depressive symptoms in adults with hypothyroidism on treatment in primary care clinics and endocrine outpatient clinics in Riyadh, Saudi Arabia.
- To define associated factors with depression adults with hypothyroidism on treatment, including family history, age, gender, marital status, work status, monthly income, level of education, co-morbid conditions, TSH and T4 levels.

Research Question

What is the prevalence and associated factors of depressive symptoms among Saudi adults with hypothyroidism on treatment in Riyadh.

Significance and Scientific Gap

Multiple studies were done worldwide about prevalence of depressive symptoms among overt hypothyroidism patients but we have no regional or local study yet. There is strong associated between depression and hypothyroidism. People with a chronic disease and on lifelong medication are more likely to have poorer mental health than those with no illnesses and certainly those on thyroxin generally have more co- morbidities like heart disease [19].

Research Hypothesis

- The prevalence of depressive symptoms among Saudi adults with overt hypothyroidism will be high as it was done among Indian adults and was estimated to be 60% [4].
- There is associated between demographic and socioeconomic characteristics of patients and depression.

Methodology

Study Design

This study was conducted using cross sectional design.

Study Setting

The study was carried out at the primary care clinics and endocrine outpatient clinics in Prince Mohammed Bin Abdul-Aziz Hospital (PMAH), in Riyadh.

Study Period

The study was conducted from 2018 to 2019 after IRB approval.

Study Subjects

Target Population

Saudi patients with overt hypothyroidism visiting primary care clinics and endocrine outpatient clinics at PMAH in Riyadh, Saudi Arabia constituted the study target population.

The Inclusion Criteria in the Study were

- Adults of both Genders.
- Patients with overt hypothyroidism on thyroxin.
- Patients who preexisting with depression after diagnosis of hypothyroidism.
- Patients who agreed to participate.

The Exclusion Criteria were

- Children and adolescents less than 18 years old.
- Patients who had overt hypothyroidism and not on treatment.
- Patients with subclinical hypothyroidism.
- Patients with a history of depression before being diagnosed with hypothyroidism.
- Patient with co morbid chronic illness except hypothyroidism.
- Patients with cognitive impairment.
- Patients who refused to participate in this study.

Sample Size

The estimated prevalence of depression in hypothyroidism is 60% with $\pm 5\%$ accuracy, confidence interval of 95% so, the estimated sample size by using a single proportion equation $N = Z^2 P(1-P)/D^2$ was 369 patients [4]. With assuming of 10% non response, the sample size was increased to 406 patients.

Sampling Techniques

Convenience sampling technique was applied to select the required patients.

Data Collection Tool

Data were collected using an interviewing questionnaire. The questionnaires are divided into 3 main parts:

- Demographic data and personal data including age, gender, level of education, work status, marital status and monthly income.
- Current and past medical history.
- The Arabic validated version of the Patient Health Questionnaire-9 (PHQ-9) for screening of depression among the participants [20]. It incorporates DSM-IV depression diagnostic criteria with other leading major depressive symptoms into a brief self-report tool. It is completed by the patient in minutes and is rapidly scored by the clinician [21]. Liu et al reported that the PHQ-9 had a good internal consistency ($\alpha = .80$) and test-retest reliability (intra-class correlation coefficient = 0.87) [22].

Scoring of PHQ-9 Responses

The PHQ-9 has 9 questions with a score ranging from 0 to 3 for each setting to consider initiating treatment with antidepressants [23]. The following table describes the provisional diagnoses for scoring classes.

PHQ-9 score	Provision Diagnosis
0-4	None
5-9	Mild Depression
10-14	Moderate Depression
15-19	Moderately Severe Depression
20-27	Severe Depression

Pilot Study

The questionnaire was tested on 10 participants to assess its applicability and estimated the time needed for its completion. As a feedback, the questionnaire was clear and approximately 8 minutes were needed to complete it.

Data Collection Management

Data were collected by interviewing each participant who met the selection criteria during regular visiting in primary care and endocrine outpatient clinics at PMAH. Random time interval was followed in each clinic during the study period.

Laboratory data (TSH and T4) were extracted from the medical information system of the hospital and added to the data collection form.

Study Variables

Independent Variables

- Age
- Gender
- Level of Education
- Marital Status
- Work Status
- Monthly Income
- Co-morbidity
- Family History of Depression
- TSH, T4 level

Dependent (outcome) Variable

Prevalence of depressive symptoms among Saudi adults with overt hypothyroidism.

Analysis Plan

- Data were analyzed using SPSS 25.0 version statistical software.
- Descriptive statistics (frequencies and percentages) were used to describe the categorical variables.
- Pearson's Chi-square test was used to assess the association between categorical variables.
- A p-value of ≤ 0.05 was used to report the statistical significance and precision of the results.

Ethical Consideration

- Approval of the study was obtained from the Institutional Review Board (IRB) in PMAH.
- Privacy and confidentiality were completely protected, No identifiers or personal information were collected or stored.
- The informed consent was clear and indicated the purpose of the study and the right of the participant to withdraw at any time without any obligation towards the study team.
- No conflict of interest.

Results

Response Rate

The study included 358 patients, out of a proposed 369 giving a response rate of 97%.

Socio-demographic Characteristics

Table 1 summarizes the socio-demographic characteristics of the participants. The age of almost one-third of them (34.1%) ranged between 30 and 39 years whereas that of 12.8% was 50 years or above. Nearly three-quarters (75.1%) of the patients were females. Majority of patients (96.1%) were Saudis. More than half of them (56%) were married. Approaching half of them (45.5%) were high school graduated whereas 31.8% had higher education. More than one-third of the participants (39.5%) were not working. The monthly income ranged between 5000 and 10000 SR/month among 55.6% of the participants.

Table 1: Socio-demographic characteristics of the participants (n=358)

	Categories	Frequency	Percentage
Age (years)	<20	27	7.5
	20-29	73	20.4
	30-39	122	34.1
	40-49	90	25.1
	≥ 50	46	12.8
Sex	Male	89	24.9
	Female	269	75.1
Nationality (n=356)	Saudi	342	96.1
	Non-Saudi	14	3.9
Marital Status (n=357)	Single	114	32.0
	Married	200	56.0
	Divorced	15	4.2
	Widow	28	7.8
Level of Education	Elementary	55	15.4
	Intermediate	26	7.3
	High school	163	45.5
	Higher education	114	31.8
Job Status/Field (n=357)	Administration	21	5.9
	Health	19	5.3
	Education	37	10.4
	Retired	14	3.9
	Not working	141	39.5
	Others	125	35.0
Monthly Household Income (SR/month)	<5000	67	18.7
	5000-10000	199	55.6
	>10000	92	25.7

Medical History

No history of medication for depression was reported among the participants. More than half (55.7%) of the participants were diagnosed with hypothyroidism since a duration ranged between one and five years whereas 15.7% of them were diagnosed since more than 10 years.

Figure 1 Thirty seven patients (10.3%) had first degree relative/s with depression. Figure 2

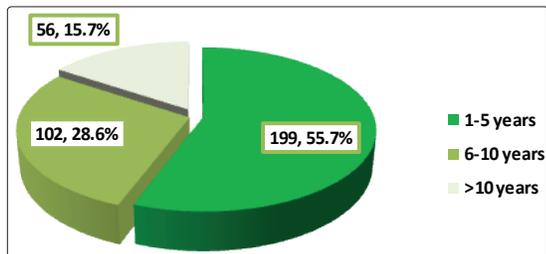


Figure 1: Duration since diagnosis of hypothyroidism among adult patients with hypothyroidism on treatment

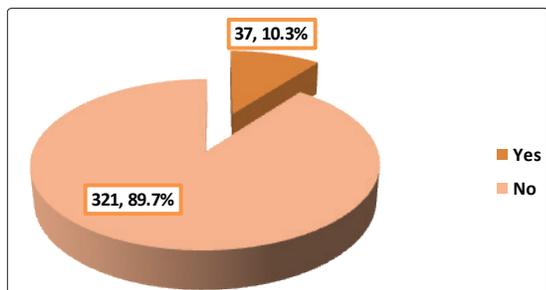


Figure 2: History of having first degree relative with depression among adult patients with hypothyroidism on treatment

Thyroid Hormones

Figure 3 shows that the level of TSH was one or more milliliters (ml) among more than half of the participants (52.1%) while figure 4 shows that T4 level was 6 or more ug/dl among 6.2% of the participants.

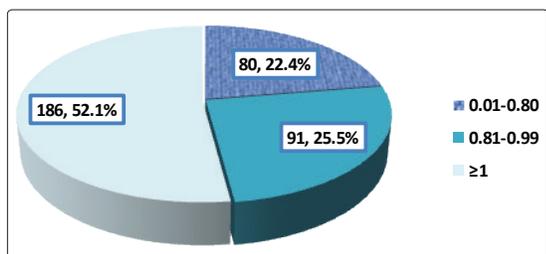


Figure 3: Level of thyroid stimulating hormone among adult patients with hypothyroidism on treatment

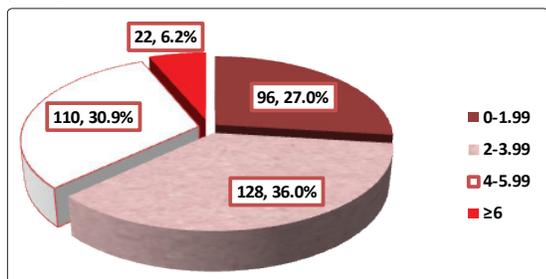


Figure 4: Level of thyroxin hormone among adult patients with hypothyroidism on treatment

Prevalence of depression among adult patients with hypothyroidism on treatment was 56.1% as shown in figure 5. It was moderately severe and severe among 58.7% and 33.3% of depressed patients,

respectively as illustrated in figure 6.

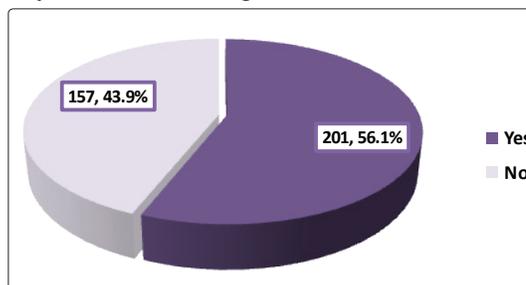


Figure 5: Prevalence of depressive symptoms among adult patients with hypothyroidism on treatment

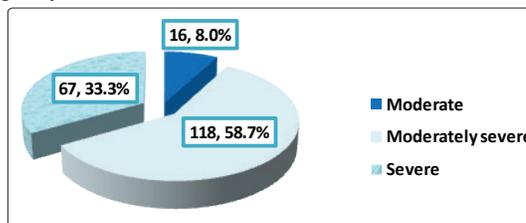


Figure 6: Severity of depression among adult patients with hypothyroidism on treatment (n=201)

Factors Associated with Depressive Symptoms Socio-demographic Characteristics

As illustrated in table 2, depression was highest reported among patients age between 40 and 49 years (66.7%) and lowest among those aged between 20 and 29 years (43.8%). Overall, the association between patient's age and depressive symptoms was statistically significant, $p=0.030$. Depressive symptoms were more significantly reported among female compared to male patients (66.5% versus 24.7%) $p<0.001$. Concerning patients' marital status, depressive symptoms was highest reported among widow (75%) and divorced patients (73.3%) and lowest reported among single patients (42.1%) $p=0.001$. Regarding patients' educational level, depressive symptoms were highest reported among elementary school educated patients (72.7%) and lowest among patients with higher education (38.6%) $p<0.001$. Patients' nationality, job status and monthly household income were not significantly associated with severity of depressive symptoms.

Table 2: Socio-demographic factors associated with depressive symptom among adult patients with hypothyroidism on treatment

	Depressive Symptoms		p-value*
	No N=157 N (%)	Yes N=201 N (%)	
Age (years)			
<20 (n=27)	13 (48.1)	14 (51.9)	0.030
20-29 (n=73)	41 (56.2)	32 (43.8)	
30-39 (n=122)	57 (46.7)	65 (53.3)	
40-49 (n=90)	30 (33.3)	60 (66.7)	
≥50 (n=46)	16 (34.8)	30 (65.2)	
Sex			

Male (n=89)	67 (75.3)	22 (24.7)	<0.001
Female (n=269)	90 (33.5)	179 (66.5)	
Nationality (n=356)			
Saudi (n=342)	151 (44.2)	191 (55.8)	0.533
Non-Saudi (n=14)	5 (35.7)	9 (64.3)	
Marital Status (n=357)			
Single (n=114)	66 (57.9)	48 (42.1)	0.001
Married (n=200)	80 (40.0)	120 (60.0)	
Divorced (n=15)	4 (26.7)	11 (73.3)	
Widow (n=28)	7 (25.0)	21 (75.0)	
Level of Education			
Elementary (n=55)	15 (27.3)	40 (72.7)	<0.001
Intermediate (n=26)	8 (30.8)	18 (69.2)	
High school (n=163)	64 (39.3)	99 (60.7)	
Higher education (n=114)	70 (61.4)	44 (38.6)	
Job Status/Field (n=357)			
Administration (n=21)	9 (42.9)	12 (57.1)	0.494
Health (n=19)	11 (57.9)	8 (42.1)	
Education (n=37)	20 (54.1)	17 (45.9)	
Retired (n=14)	7 (50.0)	7 (50.0)	
Not working (n=141)	56 (39.7)	85 (60.3)	
Others (n=125)	53 (42.4)	72 (57.6)	
Monthly Household Income (SR/month)			
<5000 (n=67)	26 (38.8)	41 (61.2)	0.602
5000-10000 (n=199)	88 (44.2)	111 (55.8)	
>10000 (n=92)	43 (46.7)	49 (53.3)	

* Chi-square test

Family History of Depression

As demonstrated from table 3, there was no statistically significant association between history of having first degree relative with depression and depression among the participants.

Table 3: Association between family history of depression and depressive symptom among adult patients with hypothyroidism on treatment

History of having First degree Relative with Depression	Depressive Symptoms		p-value*
	No	Yes	
	N157	N=201	0.139
	N(%)	N (%)	
Yes (n=37)	12 (32.4)	25 (67.6)	
No (n=321)	145 (45.2)	176 (54.8)	

* Chi-square test

Duration since Diagnosis of Hypothyroidism

Most of patients with more than ten years since diagnosis of hypothyroidism (75%) compared to 47.7% of those with a duration ranged between one and five years since diagnosis had depressive symptoms, $p < 0.001$.

Table 4: Association between duration since diagnosis of hypothyroidism and depressive symptom among adult patients with hypothyroidism on treatment

Duration since diagnosis of hypothyroidism (years)	Depressive Symptoms		p-value*
	No	Yes	
	N156	N=201	<0.001
	N(%)	N (%)	
1-5 (n=199)	104 (52.3)	95 (47.7)	
6-10 (n=102)	38 (37.3)	64 (62.7)	
>10 (n=56)	14 (25.0)	42 (75.0)	

* Chi-square test

Thyroid Hormones

It is realized from table 5 that there was no statistically significant association between levels of thyroid hormones (TST and T4) and presence of depressive symptoms.

Table 5: Association between thyroid hormones and depressive symptom among adult patients with hypothyroidism on treatment

	Depressive Symptoms		p-value*	
	No	Yes		
	N=157	N=200	0.144	
	n N(%)	N (%)		
Thyroid Stimulating Hormone (uU/ml) (n=357)				
0.01-0.80 (n=80)	37 (46.3)	43 (53.8)		
0.81-0.99 (n=91)	32 (35.2)	59 (64.8)		
≥1 (n=186)	88 (47.3)	98 (52.7)		
Thyroxin Hormone (ug/dl)				
0-1.99 (n=96)	36 (37.5)	60 (62.5)	0.515	
2-3.99 (n=128)	59 (46.1)	69 (53.9)		
4-5.99 (n=110)	50 (45.5)	60 (54.5)		
≥6 (n=22)	11 (50.0)	11 (50.0)		

* Chi-square test

Discussion

Although many studies have been conducted globally regarding the association between hypothyroidism and depression, this association still unclear and poorly defined with conflicting results [15]. Therefore this study was conducted to explore the prevalence of depressive symptoms among adults with hypothyroidism on treatment in Riyadh, Saudi Arabia and identify the factors associated with depressive symptoms among them including TSH and T4 hormonal levels.

In the present study, most of patients with overt hypothyroidism (75.1%) were females. This finding agrees with those of others who reported that overt hypothyroidism is more common among females [4,24,25].

In the current study, the prevalence of depression among adult patients with overt hypothyroidism on thyroxin treatment was 56.1%. This

prevalence is relatively high if compared with results of other similar studies carried out elsewhere. In Brazil, the prevalence of depression was 45.7% among middle aged women with hypothyroidism [10]. In Spain, the overall prevalence of hypothyroidism was 11.1% in depressive disorders [11]. In Delhi, India (2013) the prevalence of depression in patients with hypothyroidism was 36.7% [6]. In Nepal, 21% of patients with depression had thyroid dysfunction [12]. Saltevo, et al reported a prevalence of 12.5% and 17.5% among male and female patients with hypothyroidism, respectively [26]. However, it is comparable to what has been reported in another Indian study as it was 60% (56.6% among males and 64.3% among females) [4]. Also, in Italy (2012) the overall prevalence of depressive symptoms in the population with subclinical hypothyroidism was 63.5% [13].

Regarding severity of depression, it was moderately severe or severe among almost majority of patients (92%) with overt hypothyroidism in the present study. In another similar study carried out in India, depression was moderate to severe among 22.9% and 23.3% of female and male patients, respectively [4]. Chaudhary et al (2014) reported moderate to severe depression among 63% of patients with hypothyroidism also in India [25]. The difference in prevalence rate of depression and its severity between various studies could be attributed to variation in the socio-economic characteristics of patients, cultural background as well as tool used in identification of depression.

Regarding the socio-demographic factors associated with depression among patients with overt hypothyroidism on thyroxin treatment in the present study, older (≥ 40 years), female, divorced/widowed and lower educated patients were more likely to have depression. In a meta-analysis study conducted by Tang B, et al lower educated and female adults were more severely depressed than their counterparts [27]. It has been documented that educational level affects the economic and social status of patients as well as their health behavior [28].

Globally the female and male ratio of major depression is 1.7:1 [29]. The same has been confirmed in many studies [30,33]. This was attributed to biological factors, in addition to socio-economic and cultural factors [34].

The higher rate of depression among divorced and widowed compared to married patients observed in this study is confirmed by others [35,36]. In an older European study carried out in 14 countries, it was concluded that unmarried had higher rates of depression than married people [37]. Bennett et al reported that among the most negative life events is the loss of spouse [38]. The impact of loss of a spouse on life seems to be greater in females than in males [39].

In the current study, depression was more observed among patients with longer duration of overt hypothyroidism. The same has been reported by Dayan and Panicker [15]. However the explanation of this association is not clear.

The association between thyroid hormones and depression has been studied extensively and the results were not conclusive. In the present study and in agreement with other studies, no association could be found between depression and thyroid hormone levels [14,40]. However in UK, they found a clear association between higher TSH and lower free T4 and poorer psychological well-being in 697

subjects on thyroxin. The prevalence of depression in females on thyroxin was higher than that in females not on thyroxin [15,16]. In Italy, it has shown that treatment with levothyroxine alone was not sufficient to induce complete remission of symptoms of depression in population with overt hypothyroidism. Furthermore, in patients treated with T4, psychological symptoms may persist even when the euthyroid state is achieved [13].

The HUNT 2 study investigated the association between TSH and depression in more than 30,000 patients in Norway and revealed no significant association between them [41]. Similarly, in two large studies carried out in UK and Australia (in male only) no association between thyroid hormone levels and depression was found [42,43]. On the other hand, in a study carried out in USA including about seven thousands young adults, an association between lower T4 and higher TSH and depressive symptoms has been shown [44]. In another Large study conducted in UK, worse psychological well-was significantly associated with lower T4 and higher TSH in 2,269 men [45].

Strengths and Limitations of the Study

Up to our knowledge, this is the first of its kind in Riyadh to estimate the prevalence and determinants (including thyroid hormone levels) of depression among patients with overt hypothyroidism on thyroxin. However, the study has some important limitations that should be mentioned. First we included only patients with overt hypothyroidism with no control for comparison of the prevalence rate. The cross-sectional design applied in the study does not allow temporal relationship between independent and outcome variables. Inclusion of the study subjects from one health facility is another possible limitation as it could impacts the generalizability of results.

Conclusion

Depression is a very common health problem among patients with overt hypothyroidism on thyroxin treatment in Riyadh, Saudi Arabia as it affected more than half of them and majority of patients has moderately severe to severe depression. Depression was more observed among older (≥ 40 years), female, divorced/widowed and lower educated patients compared to their counterparts. Also it was more reported among patients with longer duration of hypothyroidism. No association was observed with levels of TSH and thyroxin hormones.

Recommendations

Based on the study results and their discussion, the following are recommended

- All patients with overt hypothyroid on therapy should be screened for depression by one of the commonly used scales.
- Depressed patients not responded properly to antidepressants should be screened for the thyroid status.
- Treating patients with hypothyroidism and depression early by anti-depressants as the prevalence of depression increased with increasing the duration of hypothyroidism.
- Further larger longitudinal study is recommended including patients from different health facilities in Riyadh to have more comprehensive feature of the situation.

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