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ORIGINAL ARTICLE

Depression Illness in Patients with Primary Hypothyroidism Presenting to Endocrine Clinic

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ABSTRACT

Background and Aim: Depression is associated with hypothyroidism. Somatostatin and serotonin are known to influence the hypothalamus-pituitary-thyroid axis, resulting in depression in hypothyroid patients. Neurological symptoms such as behavioral disturbances, anxiety, and depression can be associated with thyroid hormone deficiency. The present study aimed to evaluate the depression illness in primary hypothyroidism patients presented to endocrine clinics.

Patients and Methods: This descriptive cross-sectional study was carried out on 124 primary hypothyroidism patients presented to the endocrine clinic of Hayatabad Medical Complex, Peshawar during the period from February 2022 to January 2023. Patients of either gender aged >17 years and diagnosed with hypothyroidism based on T3 or T4 lower level (<1.71 pg/mL or T4 <0.7 ng/dL), higher TSH level (>4.94 uIU/mL), and TSH lower levels (<0.35 uIU/mL) were enrolled. Besides obtaining sociodemographic information, status of thyroid function status, and depression associated factors were noted. Patient Health Questionnaire (PHQ-9) was used for screening the depression among hypothyroidism patients. Moreover, the laboratory results were obtained from the patient's medical records. SPSS version 27 was used for descriptive statistics.

Results: The overall mean age was 40.16 ± 10.52 years with an age range from 18 to 70 years. There were 115 (92.7%) females and 9 (6.3%) male. About 8.2% of patients were illiterate. There were 86.7% (n=85) married. The prevalence of varying degree depression illness was 36.7% (n=36). Fatigue, hair loss, memory problem, and gland enlargement were the most prevalent depression associated symptoms. The incidence of normal, low, and elevated TSH levels were 56.1% (n=55), 7 (7.1%), and 36.8% (n=36) respectively. The most common symptoms of hypothyroidism were fatigue and reproductive issues, followed by hair loss, weight gain, thyroid gland enlargement, and cognitive difficulties. The incidence of mild, moderate, moderately severe, and severe depression was 39.8% (n=39), 12.2% (n=12), 20.4% (n=20), and 5.1% (n=5) respectively. Among hypothyroid patients, the prevalence of most stressful issues such as family, social, emotional issues, and stressful life conditions were 29 (29.6%), 22 (22.4%), 18 (18.4%), and 62 (63.3%) respectively.

Conclusion: The present study concluded that hypothyroid patients are more likely to suffer from depression and outlined the symptoms most commonly associated with depression. The incidence of depression in hypothyroid patients was 36.7%. Pregnancy, economic problems, educational problems, emotional problems, and social problems were the most common stressful situations among hypothyroid people. Patients with hypothyroidism are inclined to depression regardless of their TSH level or other risk factors such as socioeconomic problems.

Keywords: Depression, Primary hypothyroidism, Treatment-resistance depression, Patient Health Questionnaire-9

INTRODUCTION

Depression is a severe condition with a 20% lifetime probability of incidence in the United States [1]. Several variables, both modifiable and non-modifiable, raise a person's chance of getting depression, including heredity, hormone imbalances, and relationship with other medical problems [2]. Thyroid hormone imbalances can cause mood disorders such as sadness and anxiety. The incidence of affected patients for hypothyroidism and overt hypothyroidism varies from 4-40% and 1-4% respectively [3, 4]. The most recent studies reported that depression genesis could developed from brain related metabolic abnormalities that leads to the cognitive, disrupted neurotransmission, and behavior problems [5, 6]. Depression is significantly associated with hypothalamo-pituitary-thyroid (HPT) axis [7]. Hypothyroidism is the most common endocrine condition in the world [8]. It is defined as an endocrine system condition characterized by a decrease in thyroid hormone production. Age, gender, ethnicity, and iodine consumption are all variables that influence the occurrence of thyroid diseases [9]. Several studies in affluent nations showed that hypothyroidism affects 4%-5% of the global population [10, 11]. It is estimated that 5% of the US population over the age of 12 is affected [12]. Tiredness, constipation, weight gain, forgetfulness, cold intolerance, delayed speech, and sadness are all symptoms of hypothyroidism [13].

Thyroid hormone promotes the growth of neuronal processes, axons, and dendrites and enhances the rate of neuronal proliferation in the central nervous system [14]. Behavioral issues, anxiety, and depressive symptoms are induced by hypothyroidism, in turn affecting the speed of information processing, cognitive function, mood disruption, verbal fluency problems, and poor memory [15]. Depression is linked to neuroendocrine problems such as thyroid hormone imbalances. Lacking a diagnosis of subclinical hypothyroidism (SCH) can lead to sadness and delayed treatment response [16]. Many persons with depression have increased anti-thyroid antibodies [17]. Patients with chronic lymphocytic thyroiditis frequently have microsomal antibodies. Hypothyroidism can be caused by TSH impeding action caused by thyrotropin receptor (TSHR) antibodies [18]. There have been few studies to assess the depression incidence among hypothyroid patients globally, particularly in Pakistan, and all of them have been focused on researching the hypothyroid state rather than screening them for depression. Therefore, the present study aimed to evaluate the depression illness in primary hypothyroidism patients presented to endocrine clinics.

METHODOLOGY

This descriptive cross-sectional study was carried out on 124 primary hypothyroidism patients presented to the endocrine clinic of Hayatabad Medical Complex, Peshawar during the period from February 2022 to January 2023. Patients of either gender aged >17 years and diagnosed with hypothyroidism based on T3 or T4 lower level (<1.71 pg/mL or T4 <0.7 ng/dL), higher TSH level (>4.94 uIU/mL), and TSH lower levels (<0.35 uIU/mL) were

enrolled. Besides obtaining sociodemographic information, status of thyroid function status, and depression associated factors were noted. Patient Health Questionnaire (PHQ-9) was used for screening the depression among hypothyroidism patients. Moreover, the laboratory results were obtained from the patient's medical records. The specificity and sensitivity of PHQ-9 was 94% and 61% respectively. Patients has to rate from 3 (every day experience) to 0 (not at all) and each individual assigned a final score, according to which mild, moderate, moderately severe, and severe will be the varying degree of depression severity [19]. Patients with positive depression will be considered on PHQ-9 with a score ≥10. SPSS version 27 was used for data analysis. Numerical variables were expressed as mean and standard deviation whereas Categorical variables were described as frequency and percentage. All the descriptive statistics were done using 95% confidence interval and 5% level of significance.

RESULTS

The overall mean age was 40.16 ± 10.52 years with an age range from 18 to 70 years. There were 115 (92.7%) females and 9 (6.3%) male. About 8.2% of patients were illiterate. There were 86.7% (n=85) married. The prevalence of varying degree depression illness was 36.7% (n=36). Fatigue, hair loss, memory problem, and gland enlargement were the most prevalent depression associated symptoms. The incidence of normal, low, and elevated TSH levels were 56.1% (n=55), 7 (7.1%), and 36.8% (n=36) respectively. The most common symptoms of hypothyroidism were fatigue and reproductive issues, followed by hair loss, weight gain, thyroid gland enlargement, and cognitive difficulties. The incidence of mild, moderate, moderately severe, and severe depression was 44.4% (n=16), 33.3% (n=12), 16.7% (n=6), and 5.6% (n=2) respectively. Among hypothyroid patients, the prevalence of most stressful issues such as family, social, emotional issues, and stressful life conditions were 29 (29.6%), 22 (22.4%), 18 (18.4%), and 62 (63.3%) respectively. Table-1 illustrates the hypothyroidism symptoms. Figure-1 illustrates the depression levels among hypothyroidism patients. Table-II represents the stressful occurrences in hypothyroid individuals. Medical problems in hypothyroid patients are shown in Table-III. Table-IV shows the hypothyroidism patients distribution based on their demographic details. Depression and hypothyroidism-related features are associated in hypothyroid individuals are represented in Table-V. Table-VI represents the Medicines used in hypothyroid individuals that cause depression. Depression and stressful living circumstances are related with hypothyroid individuals as shown in Table-VII.

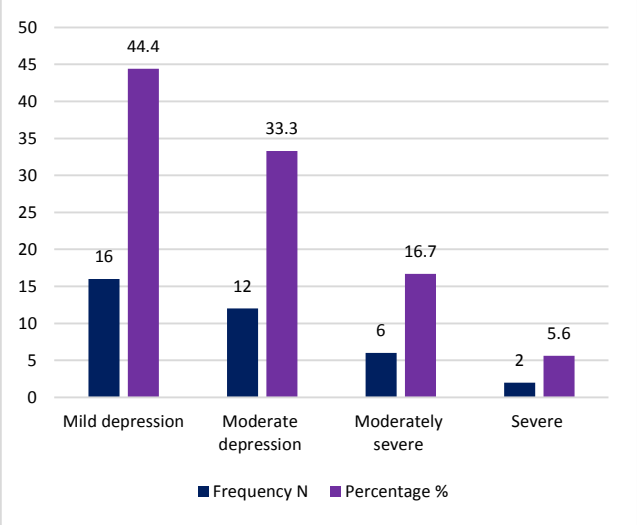

Figure-1: depression levels among hypothyroidism patients (n=36)

Table-1: hypothyroidism symptoms (n=98)

Symptoms	Yes N (%)	No N (%)
Fatigue	85 (86.7)	13 (13.3)
Reproductive issues	83 (84.7)	15 (15.3)
Hair loss	78 (79.6)	20 (20.4)
Weight gain	71 (72.4)	27 (28.6)
Thyroid gland enlargement	74 (75.5)	24 (24.5)
Cognitive problems	52 (53.1)	46 (46.9)

Table-2: stressful occurrences in hypothyroid individuals (n=98)

Stressful events	Yes N (%)	No N (%)
Family issues	29 (29.6)	69 (70.4)
Social issues	22 (22.4)	76 (77.6)
Emotional issues	18 (18.4)	80 (81.6)
Stressful life conditions	62 (63.3)	36 (36.7)
Pregnancy	9 (9.2)	89 (90.8)
Educational problems	16 (16.3)	82 (83.7)

Table-3: Medical problems in hypothyroid patients (n=98)

Diseases	Yes N (%)	No N (%)
Diabetes mellitus	18 (18.4)	80 (81.6)
Heart disease	2 (2.0)	96 (98)
Chronic kidney disease	2 (2.0)	96 (98)
Cancer	5 (5.1)	93 (92.9)
Autoimmune disease	3 (3.1)	95 (96.9)
Family history of psychiatric disease	3 (3.1)	95 (96.9)

Table-4: hypothyroidism patient's distribution based on their demographic details (n=98)

Parameters	Value or N (%)
Age (years)	40.16 ± 10.52
Gender	
Male	9 (6.3)
Females	115 (92.7)
Marital status	
Single	13 (13.3)
Married	85 (86.7)
Education	
Illiterate	8 (8.2)
Educated	90 (91.8)
Occupational status	
Working	36 (36.7)
Not working	62 (63.3)

Table-5: Depression and hypothyroidism-related features are associated in hypothyroid individuals

Features	Depressed (N=36) %	Non-depressed (N=62) %	P-value
TSH levels			0.583
Normal	56.1	43.9	
Low	7.1	92.9	
High	36.8	63.2	
Drug dose (µg)			0.77
25-100	30.9	69.1	
125-175	44.3	55.7	
200-350	31.6	68.4	

Table-6: Medicines used in hypothyroid individuals that cause depression

Medicine used	Yes N (%)	No N (%)
Beta blocker	3 (3.1)	95 (96.9)
Isotretinoin	2 (2.0)	96 (98)
Iterferon	0 (0)	98 (100)
Corticosteroid	2 (2.0)	96 (98)

Table-7: Depression and stressful living circumstances are related with hypothyroid individuals.

Conditions	Depressed (N=36) %	Non-depressed (N=62) %	P-value
Stress	37.8	25.5	0.583
No stress	62.2	74.5	

DISCUSSION

The present study mainly investigated the depression illness in primary hypothyroidism patients presented to endocrine clinics and found that the frequency of depressive disease in varied degrees was 36.7%. The most common depression-related symptoms were fatigue, hair loss, memory problems, and gland enlargement. Normal, low, and increased TSH levels were found in 56.1%, 7.1%, and 36.8% of the population, respectively. Fatigue and reproductive disorders were the most prevalent hypothyroidism symptoms, followed by hair loss, weight increase, thyroid gland

enlargement, and cognitive impairments. Depression is a prevalent issue among hypothyroid people worldwide. The incidence of depression are associated with several parameters such as demographic characteristics, social status, level of TSH, symptoms of hypothyroidism, and stressful life events.

Al-Hadi et al. [20] performed a study on 1706 major depressive disorder patients in order to evaluate the chronic SCH prevalence in MDD individuals. Severe SCH patients were more prone to mental symptoms. The higher TSH levels were due to increased BMI, depressive symptoms, advancement in age, severe anxiety, and psychotic symptoms.

Several associations between childhood trauma and thyroid anomalies were discovered in sub-analyses, modifying the relationship between depression and anxiety disorders [21]. Another study by Muhammad et al found that the around 33.9% patients had depression to varied degrees. However, the incidence of depression in the current study was 36.9%. Depression is widespread among hypothyroidism patients. Hypothyroidism patients should be examined for depression [22].

Zavareh et al. investigated 63 subclinical hypothyroidism individuals to determine the connection of depressed symptoms in SCH patients and found that depression was present in 63.5% of SCH patients, implying the significance of a psychiatric examination in SCH patients [23]. Similarly, another study conducted on 12,315 individuals by Loh et al. [24] found a relationship between SCH and depression. Consequently, hypothyroidism patients are more susceptible to depression. Tan et al. [25] carried out a study on Asian patients to investigate the association between symptoms of hypothyroidism with quality of life (QOL) and comorbidities. Quality of life was affected by dry skin, fatigue, increased comorbidities, and weakness among Asian hypothyroid patients.

Globally, the incidence of depression was estimated to be about 12.5% among hypothyroid patients in India [26]. These variations in incidence could be attributable to differences in gender, socioeconomic variables, and sample size. Working and single patients had the largest rates of depressive hypothyroid patients, with insignificant connection between marital status and depression [27]. According to our findings, people with tiredness have a significant prevalence of depression, which is followed by hair loss and weight increase. Nevertheless, only a statistically significant relationship between sadness and fatigue, memory issues, hair loss, and gland enlargement was discovered [28]. Winther et al., found a statistically significant link between TSH levels more than 10 mUI/mL and the occurrence of depressive symptoms [29]. Because of disparities in sample characteristics, the results of these research have limited generalizability.

CONCLUSION

The present study concluded that hypothyroid patients are more likely to suffer from depression and outlined the symptoms most commonly associated with depression. The incidence of depression in hypothyroid patients was 36.7%. Pregnancy, economic problems, educational problems, emotional problems, and social problems were the most common stressful situations among hypothyroid people. Patients with hypothyroidism are inclined to depression regardless of their TSH level or other risk factors such as socioeconomic problems.

REFERENCES

1. Bathla M, Singh M, Relan P. Prevalence of anxiety and depressive symptoms among patients with hypothyroidism. Indian J Endocrinol Metab 2016;20:468‐74.
2. Nuguru S P, Rachakonda S, Sripathi S, et al. (August 20, 2022) Hypothyroidism and Depression: A Narrative Review. Cureus 14(8): e28201. DOI 10.7759/cureus.28201
3. Tayde PS, Bhagwat NM, Sharma P, et al.: Hypothyroidism and depression: are cytokines the link? . Indian J Endocrinol Metab. 2017, 21:886-92. 10.4103/ijem.IJEM_265_17
4. Kotkowska Z, Strzelecki D: Depression and autoimmune hypothyroidism-their relationship and the effects of treating psychiatric and thyroid disorders on changes in clinical and biochemical parameters including bdnf and other cytokines - a systematic review. Pharmaceuticals (Basel). 2022, 15:10.3390/ph15040391.
5. Karakatsoulis GN, Tsapakis EM, Mitkani C, Fountoulakis KN: Subclinical thyroid dysfunction and major depressive disorder. Hormones (Athens). 2021, 20:613-21. 10.1007/s42000-021-00312-3
6. Shen Y, Wu F, Zhou Y, et al.: Association of thyroid dysfunction with suicide attempts in first-episode and drug naïve patients with major depressive disorder. J Affect Disord. 2019, 259:180-5. 10.1016/j.jad.2019.08.067.
7. Samuels MH: Subclinical hypothyroidism and depression: is there a link? . J Clin Endocrinol Metab. 2018, 103:2061-4. 10.1210/jc.2018-00276
8. Trifu S, Popescu A, Dragoi AM, Trifu AI: Thyroid hormones as a third line of augmentation medication in treatment-resistant depression. Acta Endocrinol (Buchar). 2020, 16:256-61. 10.4183/aeb.2020.256.
9. Jucevičiūtė N, Žilaitienė B, Aniulienė R, Vanagienė V: The link between thyroid autoimmunity, depression and bipolar disorder. Open Med (Wars). 2019, 14:52-8. 10.1515/med-2019-0008.
10. Samuels MH: Psychiatric and cognitive manifestations of hypothyroidism. Curr Opin Endocrinol Diabetes Obes. 2014, 21:377-83. 10.1097/MED.0000000000000089.
11. Lang X, Hou X, Shangguan F, Zhang XY: Prevalence and clinical correlates of subclinical hypothyroidism in first-episode drug-naive patients with major depressive disorder in a large sample of Chinese. J Affect Disord. 2020, 263:507-15. 10.1016/j.jad.2019.11.004
12. Ittermann T, Völzke H, Baumeister SE, Appel K, Grabe HJ: Diagnosed thyroid disorders are associated with depression and anxiety. Soc Psychiatry Psychiatr Epidemiol. 2015, 50:1417-25. 10.1007/s00127-015-1043-0.
13. Naseem YM, Nair A, Kumar SA, Beegum MS. Depression in Hypothyroidism and Risk Factors. Journal of Medical Science And clinical Research [Internet]. 2017;05(03):19478‐19484.
14. Moon JH, Han JW, Oh TJ, Choi SH, Lim S, Kim KW, Jang HC: Effect of increased levothyroxine dose on depressive mood in older adults undergoing thyroid hormone replacement therapy. Clin Endocrinol (Oxf). 2020, 93:196-203. 10.1111/cen.14189
15. Krysiak R, Szkróbka W, Okopień B: The effect of l-thyroxine treatment on sexual function and depressive symptoms in men with autoimmune hypothyroidism. Pharmacol Rep. 2017, 69:432-7. 10.1016/j.pharep.2017.01.005.
16. Rana H, Mirah J, Al‐Shahrani N, Nouf A, Afrah A, Basma O, et al. Incidence of thyroid diseases in female Saudi adults visiting a tertiary care hospital in Riyadh. Epidemiology2017;7:286.
17. Unnikrishnan AG, Kalra S, Sahay RK, Bantwal G, John M, Tewari N. Prevalence of hypothyroidism in adults: An epidemiological study in eight cities of India. Indian J EndocrinolMetab 2013;17:647‐52.
18. Hennessey JV, Espaillat R. Current evidence for the treatment of hypothyroidism with levothyroxine/levotriiodothyronine combination therapy versus levothyroxine monotherapy. IntJClinPract 2018;72:e13062.
19. Awad SAS, Ashraf EM, Khaled AS, Salih BS, Yousef S, Abeer AS, et al. The epidemiology of thyroid diseases in the Arab world: A systematic review. J Public Health Epidemiol 2016;8:17‐26.
20. AlHadi AN, AlAteeq DA, Al‐Sharif E, Bawazeer HM, Alanazi H, AlShomrani AT, et al. An arabic translation, reliability, and validation of patient health questionnaire in a Saudi sample. Ann Gen Psychiatry 2017;16:32.
21. Williams J, Nieuwsma J. Screening for depression in adults [Internet]. Up to date 2018. Available from: https://www.uptodate.com/home.
22. Mohammad MY, Bushulaybi NA, AlHumam AS, AlGhamdi AY, Aldakhil HA, Alumair NA, Shafey MM: Prevalence of depression among hypothyroid patients attending the primary healthcare and endocrine clinics of King Fahad Hospital of the University (KFHU). J Family Med Prim Care. 2019, 8:2708-13. 10.4103/jfmpc.jfmpc_456_19.
23. Zavareh AT, Jomhouri R, Bejestani HS, Arshad M, Daneshmand M, ZiaeiH,etal. Depression and hypothyroidism in a population‐based study of iranian women. Rom J Intern Med 2016;54:217‐21.
24. Loh HH, Lim LL, Yee A, Loh HS: Association between subclinical hypothyroidism and depression: an updated systematic review and meta-analysis. BMC Psychiatry. 2019, 19:12. 10.1186/s12888-018-2006-2.
25. Tan NC, Chew RQ, Subramanian RC, Sankari U, Koh YL, Cho LW: Patients on levothyroxine replacement in the community: association between hypothyroidism symptoms, co-morbidities and their quality of life. Fam Pract. 2019, 36:269-75. 10.1093/fampra/cmy064
26. Shivaprasad C, Rakesh B, Anish K, Annie P, Amit G, Dwarakanath CS: Impairment of health-related quality of life among Indian patients with hypothyroidism. Indian J Endocrinol Metab. 2018, 22:335-8.10.4103/ijem.IJEM_702_17.
27. LiC, ChenJ, WangW, AiM, ZhangQ, KuangL. Use of isotretinoin and risk of depression in patients with acne: A systematic review and meta‐analysis. BMJ Open 2019;9:e021549‐e.
28. Morón-Díaz M, Saavedra P, Alberiche-Ruano MP, et al.: Correlation between TSH levels and quality of life among subjects with well-controlled primary hypothyroidism. Endocrine. 2021, 72:190-7. 10.1007/s12020-020-02449-4
29. Winther KH, Cramon P, Watt T, et al.: Disease-specific as well as generic quality of life is widely impacted in autoimmune hypothyroidism and

improves during the first six months of levothyroxine therapy. PLoS One. 2016, 11:e0156925. 10.1371/journal.pone.0156925.