International Journal of Research in Medical Sciences
Harsha et al. Int J Res Med Sci. 2021 Oct;9(10):2994-2999
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20213921

Original Research Article

Thyroid dysfunction in patients of depression and anxiety and response to therapy

Harsha[1], Amandeep[1]*, Jitendera Jeenger[2], R. S. Ahlawat[3], Manju Subberwal[4]

[1]Department of Psychiatry, G. B. Pant Hospital, Maulana Azad Medical College, New Delhi, India
[2]Department of Psychiatry, Geetanjali Medical College and Hospital, Udaipur, Rajasthan , India
[3]Department of Medicine, Lok Nayak Hospital, Maulana Azad Medical College, New Delhi, India
[4]Department of Biochemistry, G. B. Pant Hospital, Maulana Azad Medical College, New Delhi, India

Received: 03 September 2021
Revised: 19 September 2021
Accepted: 18 September 2021

***Correspondence:**
Dr. Amandeep,
E-mail: dramandeeppanghal@gmail.com

ABSTRACT

Background: Depression and anxiety are the most common psychiatric presentation in thyroid dysfunction. Aim of the study was to determine the thyroid profile in patients with depressive and anxiety symptoms and to determine the change in symptoms with correction of thyroid profile.
Methods: This longitudinal observational study was conducted in patients presented with depressive or anxiety symptoms who visited the psychiatry out patient department (OPD) first time. Two groups were made based on the serum thyroid profile. First group, (n=27) was patients with depression and anxiety with hypothyroidism (experimental group) and second was (n=123) without hypothyroidism (control group). Experimental group, (n=27) was then exposed to thyroxine, 15 patients came for first follow up and 11 patients came for second follow up.
Results: The 63% of patients in the experimental group and 62.6% of patients in the control group were of female gender, 66.7% and 33.3% of patients in the experimental group had depressive disorder and anxiety disorder respectively. TSH level of 11 patients of experimental group had significantly less value in first follow up compared to entry point (p=0.002). Generalized anxiety disorder (GAD) 7 scores were significantly lower in first and second follow up than that of the entry point in 11 patients of experimental group (p=0.008, 0.016 respectively).
Conclusions: Many patients of the clinical diagnosis of depression (17.6%) and clinical diagnosis of anxiety (18.75%) had hypothyroidism during the first visit to the psychiatry OPD. There was significant reduction in the hypothyroid patients of the serum thyroid stimulating hormone (TSH) value and anxiety scores during the follow up after treatment with levothyroxine.

Keywords: Anxiety disorder, Depression, Hypothyroidism, Levothyroxine

INTRODUCTION

The association between thyroid function and behavioral disturbances has been known for the last two centuries. Although the effects of thyroid hormone on developing brain were recognized long ago, recent advances in biotechnology have led to improved understanding of the impact of thyroid functions on the adult, mature brain. This development has particularly been helpful in elucidating role of thyroid hormones in pathophysiology of psychiatric disorders, especially mood disorders.[1,2] Psychiatric disturbances are frequently observed during course of endocrine disorders. The differential diagnosis can be complex as behavioral effects of endocrinopathies often present with many different psychiatric illnesses. Psychiatric symptoms may be the first manifestations of endocrine disease, but often are not recognized as such.[3] Psychiatric syndromes associated with endocrine

dysfunction include mood disturbances, anxiety, cognitive dysfunction, dementia, delirium and psychosis.[4]

Thyroid disorders comprise a large proportion of study in endocrine disorders.[5] Depression and anxiety is the most common psychiatric presentation in thyroid disorders.[6] Both subclinical and overt thyroid disorder have been associated with mood disorders.[6]

Psychological and behavioral manifestation of hypothyroidism includes low mood, social withdrawal, impaired memory functions, apathy, and pronounced loss of interest in daily activities, poor concentration, low energy, changes in appetite and sleep disturbances. Symptoms co-occurring with hyperthyroidism include emotional lability inappropriate temper outburst, anxiety with impairment of recent memory accompanied by short attention span. In addition to this, patients may develop major depressive episodes and GAD.[7]

With the above background, psychological presentation of thyroid dysfunction especially mood and anxiety symptoms in psychiatric OPD can be better addressed by thyroid replacement therapy. Hence the study has been planned to determine the thyroid profile (TSH, FT4 and FT3) in patients with depressive and anxiety symptoms visiting the psychiatry OPD for the first time and to determine the change in depressive and or anxiety symptoms with correction of thyroid profile.

METHODS

This longitudinal observational study was conducted in patients attending the adult psychiatry outpatient services in the department of psychiatry, G. B. Pant hospital in North India between January 2019 to December 2019. Ethical clearance had been obtained from institutional ethical board of Maulana Azad medical college.

Patients with depressive or anxiety symptoms who visited the psychiatry OPD of G. B. Pant hospital for the first time. Two groups were made based on the serum thyroid profile. First group was patients with depression and anxiety with hypothyroidism (experimental group) and second was patients with depression and anxiety without hypothyroidism (control group). The sample of this study consisted of total 150 OPD psychiatric patients. Out of them, 27 patients belonged to experimental group and 123 belonged to the control group.

Inclusion criteria

Patients of either sex with depressive and or anxiety symptoms visiting for the first time in psychiatry OPD. Patients of age between 18-65 years.

Exclusion criteria

Patients with known case of thyroid dysfunction and taking any medications for thyroid disorder or medications influencing the thyroid profile (levothyroxine, propylthiouracil, glucocorticoids, propranolol, lithium, antipsychotics, tricyclic antidepressants, carbamazepine and estrogens etc.) Patient presented with severe depression, bipolar depression other major psychiatric diagnosis and co-morbid substance uses disorder other than nicotine.

Study procedure

Patients registered in the psychiatry OPD for the first time were taken up for the study as per the inclusion and exclusion criteria. Diagnosis of depression and anxiety disorders were made as per international classification of diseases (ICD-10) and validated by the psychiatrist. Out of 150 patients, 6 patients had diagnosis of mixed anxiety and depression but for the convenience of the study, it was reclassified to either depression or anxiety according to their major symptom profile. First PHQ 9 and GAD 7 rating scales were applied after taking informed consent. Then serum thyroid profile was done. Levels of TSH, FT3, FT4 were measured using electro-chemiluminescence method. Patients in whom thyroid profile was found to be deranged (serum TSH>4.2 uIU/ml), tablet thyroxine was started in a dose of 6.25 mcg-12.5 mcg under the guidance of supervisor (entry point for experimental group). First follow up of the experimental group was done after 6.60 (±3.75) weeks and the second follow up was done at after 12.36 (±6.13) weeks, after starting thyroxine. Severity of anxiety or depression was also rated on GAD 7 and PHQ 9 scales in the follow ups, respectively. Patients were also rated for subjective improvement of symptoms in percentage in the follow ups. Repeat thyroid profile was also done in the follow ups of the experimental group patients and changes were documented.

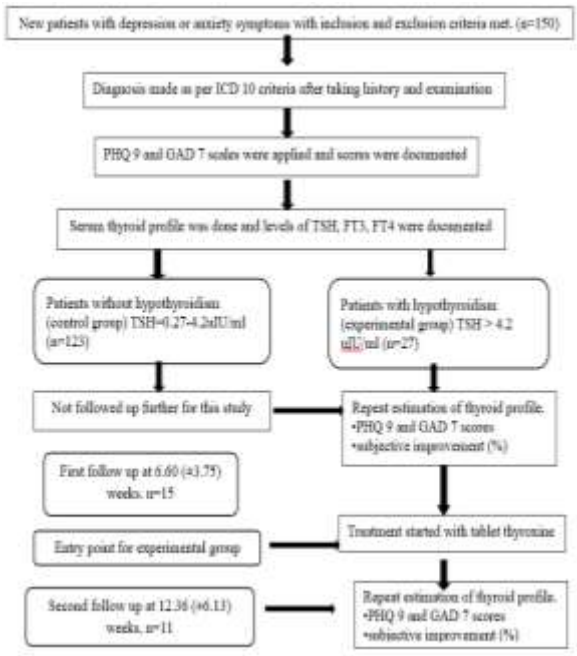

Figure 1: Flow chart of methodology.

The primary outcome measure was percentage of patients with anxiety or depressive disorders having thyroid dysfunction. The cut off for thyroid dysfunction was taken as per reference values of biochemistry laboratory of G. B. Pant hospital (i.e., TSH=0.27-4.2 uIU/ml, FT3=2-4.4 pg/ml, FT4=0.93-1.7 ng/ml). The secondary outcome measure was change in scores of PHQ 9 and GAD 7 with thyroxine, in the experimental group.

Sample size

As per previous study prevalence=35%.[8] N=87, However, to compensate for the dropouts this study took 150 patients with depressive or anxiety diagnosis.

Statistical analysis

Data were first checked for distribution with the help of Q-Q plot. Here parametric tests were used as all parameters followed near normal distributions. Categorical variables were compared between two groups (patients with normal thyroid status and patients with thyroid dysfunction) with the help of chi square test and Fisher's exact test. Similarly, continuous variables were compared with the help of student's T test. Generalized linear models were used to compare follow up data of continuous quality. Type 1 error of 5% was considered limit for significance. Charts were made with the help of excel, Microsoft office 2007. Rest of the analysis was done by IBM SPSS statistics 25.0 (International business machines).

RESULTS

Table 1 shows differences of categorical sociodemographic variables between the experimental group and control group patients at study entry. There was no significant difference between the levels of any sociodemographic variables. The 63% of patients in the experimental group and 62.6% of patients in the control group were of female gender. According to table number 2,68.3% and 31.7% of patients in the control group had depressive disorder and anxiety disorder diagnosis respectively. The 66.7% and 33.3% of patients in the experimental group had depressive disorder and anxiety disorder respectively. The 11.4% and 7.3% of patients in control group had CAD/HTN/Asthma and DM as comorbidities respectively but only 11.1% of patients in experimental group function had comorbidity in the form of CAD/HTN/asthma. 11.1% patients in experimental group and 8.1% patients in the control group had past history of psychiatric illness. None of the patients in the experimental group had family history of psychiatric illness in comparison to 13% patients in the control group (X^2=3.932, p=0.047). The 3.7% patients in the experimental group had family history of thyroid disorder compared to 10.6% patients in the control group. Table 3 shows mean GAD 7 and PHQ 9 scores at entry point were insignificantly different between the 2 groups. Mean value for GAD 7 was 9.26 at first follow up and 8.54 at second follow up of experimental group patients (n=27). PHQ 9 scores at first and second follow up of the experimental group patients were 13.46 and 12.63 respectively. In Table 4 differences among the clinical variables at their entry point, first follow up and second follow up of 11 patients of experimental group. GLM model shows significant difference among 3 follow ups in case of TSH (f=24.86, p=0.001) and GAD 7 (f=12.34, p=0.003). Other clinical variables didn't show any difference between the 3 columns. Moreover, TSH level of 11 patients of experimental group had significantly less value in first follow up compared to entry point (p=0.002). Additionally, first and second follow up values (8.90, 8.54, resp) for GAD 7 were significantly lower than that of entry point (mean=10.09) in 11 patients of experimental group (p=0.008, 0.016 respectively).

Table 1: Sociodemographic variables between the experimental group and control group patients.

Variables		Experimental group, (n=27) (%)	Control group, (n=123) (%)	X^2 (df)	Significance (p)
Gender	Male	10 (37.0)	46 (37.4)	0.001 (1)	0.972
	Female	17 (63.0)	77 (62.6)		
State	Delhi	15 (55.6)	75 (61.0)	0.271 (1)	0.603
	Others	12 (44.4)	48 (39.0)		
Residence	Urban	24 (88.9)	104 (84.6)	0.333 (1)	0.564
	Rural	3 (11.1)	19 (15.4)		
Occupation	Employed	10 (37.0)	44 (35.8)	4.685 (1)	0.196
	Homemaker	15 (55.6)	73 (59.3)		
	Student	1 (3.7)	6 (4.9)		
	Unemployed	1 (3.7)	0		
Marital status	Married	20 (74.1)	99 (80.5)	0.555 (1)	0.456
	UM/divorced/widow	7 (25.9)	24 (19.5)		
Type of family	Nuclear	26 (96.3)	111 (90.2)	1.025 (1)	0.311
	Joint	1 (3.7)	12 (9.8)		
Religion	Hindu	12 (44.4)	53 (43.1)	0.017 (1)	0.898
	Muslim	15 (55.6)	70 (56.9)		

UM- unmarried.

Table 2: Difference of clinical variables (discrete) between the experimental group and control group patients at study entry.

Variables		Experimental group, (n=27) (%)	Control group, (n=123) (%)	X^2 (df)	Significance (p)
Diagnosis	Depressive disorder	18 (66.7)	84 (68.3)	0.027 (1)	0.870
	Anxiety disorder	9 (33.3)	39 (31.7)		
Comorbidity	No comorbidity	24 (88.9)	100 (81.3)	2.131 (2)	0.345
	CAD/ HTN/Asthma	3 (11.1)	14 (11.4)		
	DM	0	9 (7.3)		
Past psychiatric history	Present	3 (11.1)	10 (8.1)	0.249 (1)	0.618
	Absent	24 (88.9)	113 (91.9)		
FH psychiatric illness	Present	0	16 (13.0)	3.932 (1)	0.047*
	Absent	27 (100.0)	107 (87.0)		
FH thyroid	Present	1 (3.7)	13 (10.6)	1.233 (1)	0.267
	Absent	26 (96.3)	110 (89.4)		

*Means p<0.05 (significant), CAD-Coronary artery disease, HTN-Hypertension, DM-Diabetes mellitus, FH-Family history.

Table 3: Differences of clinical variables (continuous) between the experimental group and control group patients at study entry

Variables	Experimental group, mean (SD), (n=27)	Control group, mean (SD), (n=123)	T (df)	Significance (p)
GAD 7 at entry	11.07 (2.71)	11.47 (3.79)	0.51 (148)	0.607
PHQ 9 at entry	13.85 (4.71)	14.60 (5.36)	0.67 (148)	0.503

GAD 7-Generalized anxiety disorder 7, PHQ 9-Patient health questionnaire 9.

Table 4: Generalized linear model of difference among entry, follow up 1 and follow up 2 values of clinical variables (n=11).

Variables	Entry	Follow up 1	Follow up 2	Within subject		Post hoc (p)
	Mean (SE)	Mean (SE)	Mean (SE)	Df (Greenhouse-Geisser)	F (p)	
TSH	7.57 (0.98)	6.07 (0.91)	5.07 (1.10)	1.23, 7.42	24.86 (0.001)*	Entry >FU1 (0.002)*
T3	2.96 (0.55)	2.40 (0.48)	3.08 (0.44)	1.14, 4.56	1.16 (0.34)	No significance
T4	2.89 (1.51)	1.72 (0.40)	1.38 (0.92)	1.06, 4.27	0.80 (0.42)	No significance
Thyroxine dose	6.66 (0.41)	7.08 (0.56)	7.08 (0.56)	1.00, 14.00	1.00 (0.33)	No significance
GAD 7	10.09 (1.04)	8.90 (0.94)	8.54 (0.82)	1.19, 11.94	12.34 (0.003)*	Entry >FU1 (0.008)* and entry >FU2 (0.016)*
PHQ 9	13.90 (1.31)	13.36 (1.34)	12.63 (1.10)	1.43 (14.37)	5.48 (0.025)*	No significance
Subjective improvement	---	8.18 (2.45)	11.18 (2.75)	1.00 (10.00)	1.50 (0.24)	No significance

*Means p<0.05 (significant), TSH-Thyroid stimulating hormone, T3-Tri-iodothyronine, T4-Tetraiodothyronine, GAD 7-Generalized anxiety disorder 7, PHQ 9-Patient health questionnaire 9, FU1-Follow up 1, FU2-Follow up 2.

DISCUSSION

Emotional and behavioral problems can be manifested due to underling medical cause like endocrinal, cardiac, neurological, immunological, gastroenterological or other chronic medical diseases. Endocrinal especially hypothyroidism is manifested as low mood, poor concentration, lack of energy, sleep problems, appetite changes, cognitive slowing or sometimes anxiety issues. This study was design to find out the thyroid profile

(TSH, FT4, FT3) in patients with depressive and anxiety symptoms visiting the psychiatry OPD for the first time and to determine the change in depressive and or anxiety symptoms with correction of thyroid profile.

Both the experimental group and control group was dominated by female gender. However, literature reports thyroid disorder to be more common in females.[9] This finding could be because of depressive and anxiety symptoms are commonly found in female gender.[10, 11]

At the entry of this study, 119 patients (79.3% of the total 150 patients) had depression according to PHQ 9. Thirteen out of them, (additional 2 patients entered into the first follow up after being diagnosed with hypothyroidism who did not have PHQ 9 based depression diagnosis) came for first follow up and 9 out of 13 came for the second follow up (same two additional patients followed up second time because they were hypothyroid). PHQ 9 score shows overall improvement in follow ups (p=0.025) but post hoc test could not differentiate between any two scores. Significant, improvement was seen in GAD 7 score over follow up 1 and 2 from entry point (p=0.008, p=0.016). Nine patients who were diagnosed moderate anxiety according to GAD 7 (out of 15 patients of entry and first follow up) when followed up for the first time, 2 out of them showed minimal or no anxiety based on GAD 7. Similarly, 4 patients (out of 11 patients of follow up 2) who had moderate anxiety based on GAD 7 at first follow up when followed up second time none of them had changed their severity from moderate to minimal or no anxiety.

As far as the impact of levothyroxine treatment on anxiety and depressive symptoms is concerned, although depression and anxiety both reduced significantly in follow ups but diagnosis of depression (PHQ 9 based) and moderate anxiety (GAD 7 based) did not change in the follow ups (except 2 patients of anxiety in the first follow up). TSH in this study reduced significantly in follow ups (p=0.001). One of the Indian studies, Vishnoi et al taking 300 subclinical hypothyroidism patients showed significant fall in the level of TSH with HAM D score after levothyroxine treatment.[12]

Rogers et al observed higher rates of medical illness in mixed panic disorder and depression patients compared to only anxiety patients without depression.[13] Sareen et al showed 64% of their anxiety patients to have thyroid dysfunction.[14] Similarly, Simon et al examined thyroid dysfunction in different anxiety disorders and found 6.5% in panic disorder and 10.4% in generalized anxiety disorder.[15] In our study, we found 18% (27 patients out of 150) of our OPD patients presented with anxiety and depressive symptoms having hypothyroidism. When we divided these 18% (27 patients) patients according to clinical diagnosis, we found 66.6% patients had clinical depression diagnosis and 33.3% patients had clinical anxiety disorder diagnosis. Radhakrishnan et al found 23.24% hypothyroidism in mood disorder patients.[16] They included both unipolar and bipolar depression but we took only unipolar depression. Similarly, Ojha et al found thyroid dysfunction in 21% of depressed patients.[4] Our study observed hypothyroidism in 17.6% of the clinically diagnosed depressed patients and 18.75% of the clinically diagnosed anxiety patients. Some of the studies also calculated the proportion of patients having subclinical hypothyroidism (11.4% of depressed patients of Ojha et al 22% of mood disorder patients of Chhetry et al.[4,17] But we did not report any subclinical hypothyroidism separately, rather we considered hypothyroidism in any case where TSH >4.2 uIU/ml.

Bensenor et al observed 2.55 times more prevalence of sub-clinical hyperthyroidism in panic disorder.[18] Witthauer et al reported 1.72 times more thyroid disease in specific phobias. But in our study, we didn't divide anxiety disorder into subcategories.[19]

Limitation of our study is that for better interpretation randomized control trail in needed. More validated instruments like Hamilton anxiety rating scale or Hamilton depression scale can be used. Many studies observed subclinical hypothyroidism as the outcome variable but we do not include subclinical hypothyroidism.

CONCLUSION

It was an open label follow up study with standard treatment of hypothyroidism in psychiatric patients with anxiety and depressive symptoms. The 17.6% patients of the clinical diagnosis of depression and 18.75% of the clinical diagnosis of anxiety had hypothyroidism. There was significant reduction in the hypothyroid patients of the serum TSH value and anxiety scores during the follow up after treatment with levothyroxine. Although the depression score of the hypothyroid psychiatric patients was reduced in the follow up but post hoc analysis was insignificant. It has been suggested to assess the serum thyroid profile in female psychiatric patients especially those without family history of psychiatric illness presenting with anxiety and depressive symptoms and to treat, if hypothyroidism detected, so as to improve some of the depressive and anxiety symptoms.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Porterfield SP, Hendrich CE. The role of thyroid hormones in prenatal and neonatal neurological development-current perspectives. Endocrine reviews. 1993;14(1):94-106.
2. Bernal J, Nunez J. Thyroid hormones and brain development. Eur J Endocrinol. 1995;133(4):390-8.

3. Geffken GR, Ward HE, Staab JP, Carmichael SL, Evans DL. Psychiatric morbidity in endocrine disorders. Psychiatr Clin North Am. 1998;21(2):473-89.
4. Ojha SP, Dhungana S, Chapagain M, Tulachan P. Association of thyroid dysfunction with depression in a teaching hospital. J Nepal Health Res Counc. 2013;11(23):30-4.
5. Sartorius N, Ustun TB, Lecrubier Y, Wittchen HU. Depression comorbid with anxiety: results from the WHO study on psychological disorders in primary health care. Br J Psychiatry. 1996;168 (S30):38-43.
6. Sapini Y, Rokiah P. Thyroid disorders and psychiatric morbidities. Malaysian J Psychiatry. 2009;18:2.
7. Khouzam HR, Weiser PM, Gill T, Raroque R. Thyroid hormones therapy: A review of their effects in the treatment of psychiatric and medical conditions. Comprehensive therapy. 2004;30(3):148-54.
8. Sakai Y, Iversen V, Reitan SK. FT4 and TSH, relation to diagnoses in an unselected psychiatric acute-ward population, and change during acute psychiatric admission. BMC psychiatry. 2018;18(1):244.
9. Ralston S, Penman I, Strachan M, Hobson R. Davidson's Principles and Practice of Medicine. 23rd ed. Elsevier. 2018.
10. Akiskal SH. Mood disorders: historical introduction and conceptual interview. In: Sadock BJ, Sadock VA, Ruiz P. Kaplan and Sadock's Comprehensive Textbook of Psychiatry 10th ed. Lippincott William and Wilkins. 2017.
11. Merikangas KR, Eun JD. Epidemiology of Anxiety Disorders. In: Sadock BJ, Sadock VA, Ruiz P. Kaplan and Sadock's Comprehensive Textbook of Psychiatry.10th ed. Lippincott William and Wilkins. 2017.
12. Vishnoi G, Chakraborty B, Garda H, Gowda SH, Goswami B. Low mood and response to Levothyroxine treatment in Indian patients with subclinical hypothyroidism. Asian J Psychiatr. 2014;8(1):89-93.
13. Rogers MP, White K, Warshaw MG, Yonkers KA, Rodriguez-Villa F, Chang G et al. Prevalence of medical illness in patients with anxiety disorders. Int J Psychiat Med. 1994;24(1):83-96.
14. Sareen J, Jacobi F, Cox BJ, Belik SL, Clara I, Stein MB. Disability and poor quality of life associated with comorbid anxiety disorders and physical conditions. Arch Intern Med. 2006;166(19):2109-16.
15. Simon NM, Blacker D, Korbly NB, Sharma SG, Worthington JJ, Otto MW et al. Hypothyroidism and hyperthyroidism in anxiety disorders revisited: new data and literature review. J Affect. 2002;69(1-3):209-17.
16. Radhakrishnan R, Calvin S, Singh JK, Thomas B, Srinivasan K. Thyroid dysfunction in major psychiatric disorders in a hospital-based sample. Indian J Med Res. 2013;138(6):888.
17. Chhetry MG, Sapkota N, Ojha N, Thapa S, Pandey AK. Association of Thyroid Dysfunction with Mood Disorders in an OPD setting. J Psychiatrists' Association Nepal. 2014;3(1):23-8.
18. Bensenor IM, Nunes MA, Sander Diniz MD, Santos IS, Brunoni AR, Lotufo PA. Subclinical thyroid dysfunction and psychiatric disorders: cross-sectional results from the Brazilian Study of Adult Health (ELSA-Brasil). Clin endocrinol. 2016;84(2):250-6.
19. Witthauer C, Ajdacic-Gross V, Meyer AH, Vollenweider P, Waeber G, Preisig M et al. Associations of specific phobia and its subtypes with physical diseases: an adult community study. BMC psychiatry. 2016;16(1):155.

Cite this article as: Harsha, Amandeep, Jeenger J, Ahlawat RS, Subberwal M. Thyroid dysfunction in patients of depression and anxiety and response to therapy. Int J Res Med Sci 2021;9:2994-9.