ISSN Print: 2394-7500
ISSN Online: 2394-5869
Impact Factor: 5.2
IJAR 2019; 5(12): 52-56
www.allresearchjournal.com
Received: 26-10-2019
Accepted: 29-11-2019

Dr. Nita Sahi
Associate Professor, Department of Biochemistry, Pacific Medical College & Hospital, Udaipur, Rajasthan, India

Dr. Sangeeta Gurjar
PG Student, Department of Biochemistry, Pacific Medical College & Hospital, Udaipur, Rajasthan, India

Dr. Jafar Khan
Research Scholar, Department of Microbiology, Pacific Institute of Medical Sciences, Udaipur, Rajasthan, India

Dr. Ashutosh Meena
PG Student, Department of Biochemistry, Pacific Medical College & Hospital, Udaipur, Rajasthan, India

Dr. Gautam Kumar Sharma
PG Student, Department of Biochemistry, Pacific Medical College & Hospital, Udaipur, Rajasthan, India

Correspondence Author:
Dr. Jafar Khan
Research Scholar, Department of Microbiology, Pacific Institute of Medical Sciences, Udaipur, Rajasthan, India

Correlation of anxiety disorder with serum TSH and Cortisol level in young adults

Dr. Nita Sahi, Dr. Sangeeta Gurjar, Dr. Jafar Khan, Dr. Ashutosh Meena and Dr. Gautam Kumar Sharma

Abstract
Aim and Objective: Significance of TSH and Serum Cortisol in patient of anxiety disorder in young adults.
Introduction: Anxiety disorders refer to a group of mental disorders characterized by feelings of anxiety and fear, including generalised anxiety disorder (GAD), panic disorder, phobias, social anxiety disorder, obsessive-compulsive disorder (OCD) and post-traumatic stress disorder (PTSD). As with depression, symptoms can range from mild to severe. The duration of symptoms typically experienced by people with anxiety disorders makes it more a chronic than episodic disorder. Variations and hormonal level also play significant role in GAD.
Materials and Methods: Detailed data was collected regarding age, occupation, marital status, special habits, smoking and alcohol intake, vegetarian and non vegetarian status, family size status, duration of disease, associated complications, associated medical and surgical conditions, and drug intake.
Serum TSH and Cortisol level was detected by standard procedure taking sample from patients under study
Results and Discussion: In our study all (100%) participants were young adults. None of the individual was below 15 years of age in this study. Most (45.7%) of the participants belonged to age group of 25-30 years, 65.7% of individuals were male, while 34.2 % were females. Male predominance was seen. Mean RBS of cases was 116.32±17.14 while in control mean RBS is 113.17±18.07. Mean value of TSH in cases is 1.32±0.32 and in control mean TSH is 2.48±0.99.Mean value of Serum cortisol in cases is 295.83±100.27and in control mean cortisol is 122.76±77.10. The difference between values of Serum Cortisol and Serum TSH in case and control is found statistically significant ($P<0.05$). The vast majority of patients with hyperthyroidism will display a psychiatric disorder such as anxiety, mania, or depression and Cortisol level also play important role in the same.
Conclusion: Thus it can be concluded that low level of TSH and high level of cortisol responsible for anxity disorders in adults under study some of the socio- demographic factors like family history.

Keywords: TSH and Cortisol level, socio- demographic factors

Introduction

Anxiety disorders are common and distressing medical conditions, which typically arise in adolescence or early adult life. Anxiety disorders refer to a group of mental disorders characterized by feelings of anxiety and fear, including generalised anxiety disorder (GAD), panic disorder, phobias, social anxiety disorder, obsessive-compulsive disorder (OCD) and post-traumatic stress disorder (PTSD). As with depression, symptoms can range from mild to severe. The duration of symptoms typically experienced by people with anxiety disorders makes it more a chronic than episodic disorder (Szpunar and Parry, 2018) [1].

Age-associated alterations in hypothalamic–pituitary–adrenal (HPA) axis functioning may make individuals more susceptible to HPA dysregulation in the context of mood and anxiety disorders. Little to no research has been done to examine HPA axis function in generalized anxiety disorder (GAD), particularly in late-life GAD, the most prevalent anxiety disorder in the elderly (Mantella *et al.*, 2008) [2, 18]. Similarly, anxiety states frequently occur in association with thyroid diseases including hyper- and hypo-thyroidism and thyroiditis in addition to other endocrine disorders such as Cushing's disease, hyperparathyroidism, hyperglycemia and so on (Hall and Hall, 1999) [3]. Hyperthyroidism (Jefferson *et al.*, 1981) [4], hypothyroidism and thyroiditis have been identified as the medical illnesses most often associated with

anxiety symptoms and most frequently misdiagnosed as a primary anxiety disorder (Hall, 1980) [5].

Several Studies investigating cortisol and TSH secretion in patients with generalized anxiety disorder (GAD) have reported heterogeneous findings (Kern *et al.*, 2008) [6]. Further, current knowledge on the specificity of endocrine changes for GAD and/or comorbid major depression (MD) is limited.

Hence, in the present study attempt has been made to determining the relationship between GAD and long-term integrated cortisol secretion as well as TSH experimentally-induced cortisol stress reactivity.

Materials and methods

Study Area: Study was conducted in department of biochemistry in Pacific Medical College and Hospital, Udaipur district.

Study Design: Types of study is case control study

Study period: March 2019 September 2019.

Sample Population: GAD patients attended PMCH Udaipur Dist. Fulfilling all the inclusion criteria.

Sample size: For this study sample size of 35 for each group after roundup.

Inclusion criteria

This observation study is a type of case control study which is institution based, Data was collected after getting ethical clearance from committee.

A total of 70 GAD cases/controls of 15-30 years age were selected attending Pacific medical college and hospital, Udaipur, Rajasthan. They were studied under two group.

Group I: - It were consist of healthy control subjects (n=35). Subjects are healthy it was ensured by routine tests. All the subjects included in this group were healthy and there are no signs and symptoms or history of chronic diseases

Group II: - It were consist of GAD subject case (n=35), have symptoms which is diagnosed by psychiatrist.

Exclusion criteria

- Subjects below 15 years and above 30 years of age were excluded in the study.
- Subjects with metabolic diseases, malnutrition, or histories of consuming vitamins or mineral supplements were excluded from the study.
- Cancer patients.
- Diabetes mellitus, liver or kidney diseases or infection patients.
- Pregnant women

Source of data

Data was collected from department of Biochemistry Pacific Medical College and Hospital, Udaipur, and Rajasthan after obtaining PMCH ethical committee permission. Patients attending OPD and IPD of psychiatry department of Pacific hospital associated with Pacific medical college and Hospital, Udaipur were included in this study.

On the basis of the inclusion and exclusion criteria 35 cases and 35 controls of age and sex matched individuals were involved in the present study after obtaining informed consent. A pre-tested proforma was used to record relevant information (patient's data, investigation reports, etc.)

Methods of collection of data

Detailed data was collected regarding age, occupation, marital status, special habits, smoking and alcohol intake, vegetarian and non-vegetarian status, family size status, duration of disease, associated complications, associated medical and surgical conditions, and drug intake.

Blood collection, separation and storage of sample

Each participant was assigned with unique ID number same was mentioned on sample container. After obtaining informed consent from all patients and healthy control, 5 ml of venous blood was collected in a sterile plain bulb under all aseptic precautions. Blood was drawn from anticubital vein in plain vial. After samples collection, samples were centrifuged in REMI centrifuge at 3000 RPM for a period of 15 minutes at central laboratory of Pacific Hospital. Serum was separated after centrifugation. Serum was kept at -20^{0}C (for cortisol) until assayed. While analyzed for the following parameters:-

1. Thyroid stimulating Hormone (TSH by ECLIA method)
2. Cortisol (by ELSIA)

Statically analysis: Data thus collected was incorporated to microsoft Excel sheet in the form of master chart and was analyzed by using standard statistical software (SPSS version 20). Significance testing for Mean ±SD difference of two groups was done by student T- test (unpaired t- test). Qualitative data was compared using chi square test. p-value < 0.05 was considered statistical significant.

Results and discussion

Anxiety disorders can be linked to chemical imbalances in the body, along with other physiological factors such as sleep, diet, and exercise. So too, hormone imbalances can also reduce or increase your anxiety.

In this hospital based Case Control study assessment was made on relationship between various parameters including Cortisol and TSH in GAD patients attending Psychiatry Department of the Pacific Medical College and Hospital Udaipur, Rajasthan.

Present study comprised of 35 cases of GAD and 35 controls, who attended the psychiatry department in pacific medical college and hospitals. All study participants were included fulfilling inclusion criterion from age group between 15-30 years.

In present study all (100%) participants were young adults of 15-30 years of age. Most (45.7%) of the participants belonged to age group of 25-30 years, followed by 15-20 years (22.8). Mean age of case and control was 24.6 and 24.3 respectively which was almost similar, which shows that both group were comparable. Walter *et al.* (2012) suggested a positive relationship between TSH and cortisol in apparently healthy young individuals. In as much as this relationship may herald a pathologic disorder, these preliminary results suggest that TSH levels > 2.0 uIU/L may be abnormal.

Results reveals that 65. 7% of patients were male, whereas 34.2 % were females. Male predominance seen in samples overall but males and females are nearly have equal distribution in case and control. Meng *et al.* (2015) [8] studied the correlation Gender and age had substantial influence on thyroid function and MS. Females with high TSH and high FT3 had higher MS risks than males. Aging

was a risk for MS, especially for females. Urgent need is necessary to initiate interventional programs.

Results depicted that 52.85% of individuals were married and 47.14% were unmarried. 48.57% of cases were observed to be married while 57.14 % individuals were married in control group. Maximum number of individuals incorporated in this was students i.e. 42.85%.Whereas numbers of working and housewives were similar i.e. 28.57. So GAD is more common during student period of life. Similar evidence were also given by Hackney and Dobridge (2009) [9].

Majority of study individuals were Hindu (74.2%) followed by muslims (14.2%) and then jains (11.4%). Results depicted that most (57.14%) of the participants were from urban areas, followed by rural (25.71%) and tribal (17.14%). As our center is situated in urban area and preferred by urban population nearby, so results showing urban area predominance cannot be firmly ascertained. But if it is true unplanned urbanization, migration from rural areas, education pressure with lack of job opportunities may be some suggested possible reasons (Parry, 2000) [10]. Data revealed that maximum of participants were vegetarian (54.2%). Non vegetarian diet is distributed differently as in cases (45.7%) and in control (34.2%).

Results also showed that 68.5 % of individual possess no history of smoking. Among all cases 31.4% gave a positive history of smoking. In case of control maximum individuals were nonsmokers.

In drinking habits it was found that 42.8 % of cases were alcoholic and 34.28 % controls were alcoholic. While 57.1% cases were non-alcoholic as compared to control. Rachdaoui and Sarkar (2013) [11] studied that Chronic consumption of a large amount of alcohol and smoking disrupts the communication between nervous, endocrine and immune system and causes hormonal disturbances that lead to profound and serious consequences at physiological and behavioral levels. These alcohol-induced hormonal dysregulations affect the entire body and can result in various disorders such as stress abnormalities, reproductive deficits, body growth defect, thyroid problems, immune dysfunction, cancers, bone disease and psychological and behavioral disorders.

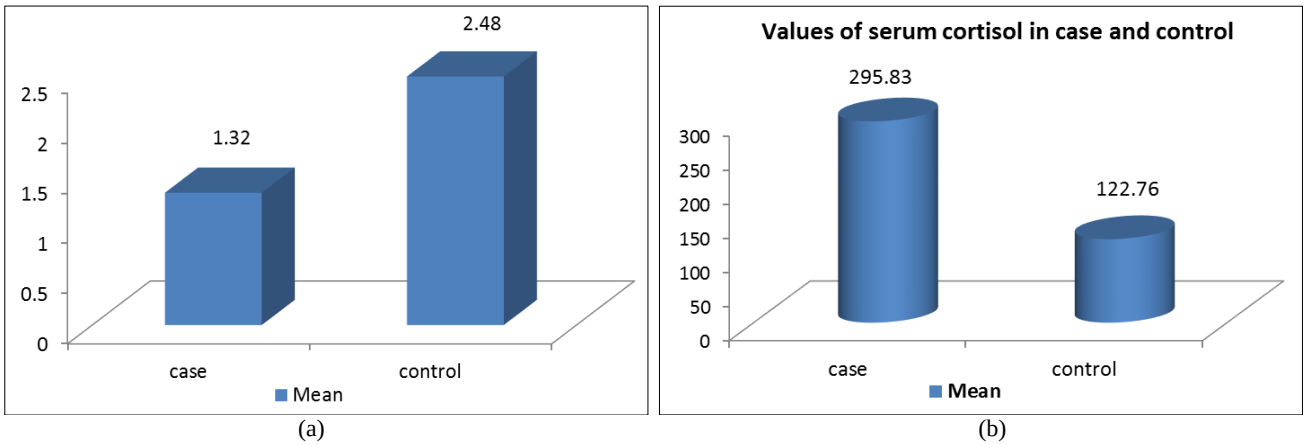
In addition results shows that 51.4% of cases complained of reduced sleep while in control subjects sleep was adequate in majority of (68.5%) patients. There is no significant difference between sleep adequacy in cases and control group. According to a study by Balbo *et al.* (2010) [12] Abrupt shifts of the sleep period induce a profound disruption in the daily cortisol rhythm, while sleep deprivation and/or reduced sleep quality seem to result in a modest but functionally important activation of the axis. HPA hyperactivity is clearly associated with metabolic, cognitive and psychiatric disorders and could be involved in the well-documented associations between sleep disturbances and the risk of obesity, diabetes and cognitive dysfunction. Several clinical syndromes, such as insomnia, depression, Cushing's syndrome, sleep disordered breathing (SDB) display HPA hyperactivity, disturbed sleep, psychiatric and metabolic impairments.

Data also shows that 48.5% of cases complained of reduced appetite while in control subjects appetite was good in 71.4% of individuals. Sleeping and feeding are intricately related. Animals faced with food shortage or starvation sleep less (Danguir and Nicolaidis, 1979) [13]; Conversely, animals subjected to total sleep deprivation for prolonged periods of time increase their food intake markedly (Everson *et al.*, 1989) [14]. Recent studies in humans have shown that the levels of hormones that regulate appetite are profoundly influenced by sleep duration. Sleep loss is associated with an increase in appetite that is excessive in relation to the caloric demands of extended wakefulness.

In among the all cases, 51.4% of cases had positive family history of similar illness while in control subjects only 25.7% individual had family history of similar illness. There were significant differences observed between two groups. This observation may be indicative of some roll of genetic causes in case of GAD.

It was observed that mean systolic BP of cases is 116.32±8.9and while in control mean systolic BP is 118.2±8.3. Result revealed that there was significant difference (P 0.041) in pulse between cases (82.53±6.82) and control (88.31±10.13). Data showed that mean Random Blood Sugar of cases was 116.32 while in control mean RBS was 113.

Results showed that mean value of TSH in cases and control was 1.32±0.32 and 2.48±0.99 respectively. The difference between values of TSH in case and control was found to be statistically significant (P=0.001).



(a) (b)

Fig 1: (A) Mean values of TSH (B) Mean values of Cortisol)

Results showed that mean value of Serum cortisol in cases and control was 295.83 and 122.76ng/mL respectively. The difference between values of serum cortisol in case and control is found statistically significant.

The interpretation of these data is difficult because analysis of many studies demonstrate that not all patients with GAD have hypercortisolism, and not all patients with hypercortisolism have GAD.

Chaudhary *et al.* (2020) [15] also studied that Females of reproductive age group with clinical and subclinical hypothyroidism faced the same amount of stressful life events. However, their perception of stress was significantly different. High TSH was positively correlated with high score on PSS. Clinical hypothyroidism is associated with hypercortisolemia and also depression. However, a cause–effect relation is yet to be established. Moreover, depression and serum cortisol were not assessed, so no further conclusions can be drawn from the present study.

Generalized Anxiety Disorder (GAD) is a common and impairing anxiety disorder in older adults (Bryant *et al.*, 2008; Wetherell *et al.*, 2004) [16, 17], and it has been associated with elevated cortisol in this age group (Mantella *et al.*, 2008; Chaudieu *et al.*, 2008) [2, 18, 19].

This is not a simple aging effect because it is absent in healthy volunteers. The potentiating or additive effect of age in conjunction with persistent Anxiety depression on pituitary adrenocortical activity was suggested by other studies.

Close reading of the literature show there is striking that HPT axis alterations and hypercortisolism have almost exclusively been described in in-patients (Weber 2000) [20], and to a much lesser extent in outpatients.

Young *et al.* (1991) [21] and Sullivan (1997) [22] suggest that the in/outpatient status is an important factor in the presence of endocrine alterations in major depression following GAD.

Results shows that mean value of TSH in male cases and control was 1.31±0.24 and 2.46±0.87 respectively. The difference between values of TSH in male cases and control is found statistically significant (P=0.001). In case of females TSH was raised in controls (2.58) than cases (1.79) and difference was found statistically significant (p<0.019). Data revealed that mean value of cortisol in male cases was 310.31±51.74 in male control mean cortisol is 99.40±21.7. In females also cortisol was raised in cases (248.21±132.01) than controls (180.32±69.17). The difference was found statistically significant in both cases and control.

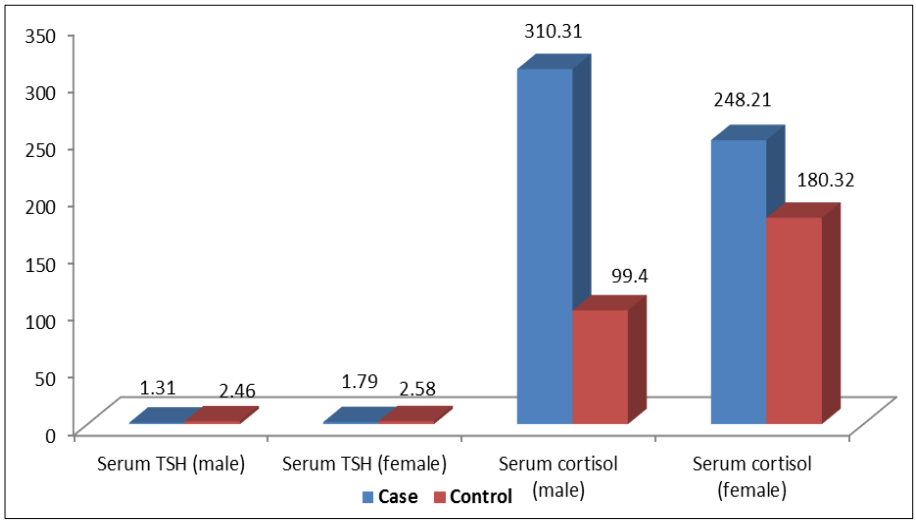


Fig 2: Aggregate representation of all important biochemical parameters

Data shows that there is low level of serum TSH and raised level of serum cortisol in cases than compare to controls in both male and female participants.

The vast majority of patients with hyperthyroidism will display a psychiatric disorder such as anxiety, mania, or depression (Chakrabarti, 2011) [23]. Between 30% and 40% present with conspicuous complaints of anxiety, nervousness, apprehension, dread, depression, restlessness, diminished concentration, forced thinking, emotional lability, and hyperkinesia. The occurrence of anxiety as a symptom of hyperthyroidism is well recognized. In one study, 29 patients were prospectively followed and found that 23 of them were diagnosed with generalized anxiety disorder and/or panic disorder. [94]

Regarding diurnal profiles of cortisol, Mantella *et al.* (2008) [2, 18] demonstrated that patients diagnosed with GAD displayed increased Serum Cortsol levels and higher peak cortisol compared with control subjects. Furthermore, severity of GAD symptoms was associated with Serum Cortisol secretion. However, findings concerning baseline alterations are inconsistent with studies attempting to replicate these results as done by Lenze EJ *et al.* (2011) [24] and studies that did not detect group differences. Considering comorbid MDD, one trial failed to detect an influence of depression on the extent of cortisol release in GAD done by Mantella *et al.* (2008) [2, 18]. This finding was supported by the results of Lenze *et al.* (2011) [24]. Although they did not control for the presence or the magnitude of MDD, the GAD sample investigated showed a comparable severity of depression and significantly elevated basal cortisol levels compared with healthy controls However, due to the small number of studies addressing this topic, these conclusions should be considered preliminary.

Challenge paradigms in another trial, cortisol levels of 30 GAD patients and 30 controls were comparable in the suppressor and nonsuppressor groups after administration of 1mg dexamethasone by Tiller *et al.* (1988). Pomara *et al.* (2005) [25] did not find baseline differences between GAD patients and healthy controls.

Thus it can be concluded that most of the cases were married and belongs to urban area. The baseline characters, activity and other sign and symptoms were similar and mostly differences between them were statistically not significant except pulse rate. There was also observed

important risk factors and family history to correlate any socio-demographic characteristic making difference in pathophysiology of GAD. But only family history was found statistically significantly related. Serum TSH and Serum Cortisol were measured and we found significantly low levels of serum TSH and raised level of serum Cortisol in GAD cases.

References

1. Szpunar MJ, Parry BL. A systematic review of cortisol, thyroid-stimulating hormone, and prolactin in peripartum women with major depression. Arch Womens Ment Health. 2018; 21(2):149-161. doi:10.1007/s00737-017-0787-9
2. Mantella RC, Butters MA, Amico JA *et al.* Salivary cortisol is associated with diagnosis and severity of late-life generalized anxiety disorder. Psychoneuroendocrinology. 2008; 33(6):773-781.
3. Hall RCW, Hall RCW. Anxiety and Endocrine Disease. Seminars in Clinical Neuropsychiatry, 1999. Available at drrichardhall.com
4. Jefferson JW, Marshal JR, editors. Neuropsychiatric features of Medical Disorders, New York: Plenum, 1981, 6-7.
5. Hall RCW. Anxiety. In Hall RCW, editor. Psychiatric Presentations of Medical Illness. New York: Spectrum, 1980, 13-35.
6. Kern S, Oakes TR, Stone CK *et al.* Glucose metabolic changes in the prefrontal cortex are associated with HPA axis response to a psychosocial stressor. Psychoneuroendocrinology. 2008; 33:517-529.
7. Walter KN, Corwin EJ, Ulbrecht J *et al.* Elevated thyroid stimulating hormone is associated with elevated cortisol in healthy young men and women. Thyroid Res. 2012; 5(1):13. Published 2012 Oct 30. doi:10.1186/1756-6614-5-13
8. Meng Z, Liu M, Zhang Q *et al.* Gender and Age Impacts on the Association between Thyroid Function and Metabolic Syndrome in Chinese. Medicine (Baltimore). 2015; 94(50):e2193. doi:10.1097/MD.0000000000002193
9. Hackney AC, Dobridge JD. Thyroid hormones and the interrelationship of cortisol and prolactin: influence of prolonged, exhaustive exercise. Endokrynol Pol. 2009; 60(4):252-257.
10. Parry BL. Hormonal Basis of Mood Disorders in Women. In: Frank, E. (Ed.), Gender and Its Effects on Psychopathology. Washington, DC. American Psychopathological Association, 2000, 3-22.
11. Rachdaoui N, Sarkar DK. Effects of alcohol on the endocrine system. Endocrinol Metab Clin North Am. 2013; 42(3):593-615. doi:10.1016/j.ecl.2013.05.008
12. Balbo M, Leproult R, Van Cauter E. Impact of sleep and its disturbances on hypothalamo-pituitary-adrenal axis activity. Int J Endocrinol. 2010; 2010:759234. doi:10.1155/2010/759234
13. Danguir J, Nicolaidis S. Dependence of sleep on nutrients' availability, Physiol Behav. 1979; 22:735-740.
14. Everson CA, Bergmann BM, Rechtschaffen A. Sleep deprivation in the rat: III: total sleep deprivation. Sleep. 1989; 12:13-21.
15. Chaudhari A, Koner S. A study of correlation of perceived stress and thyroid function among females in rural population of reproductive age group. Med JDY Patil Vidyapeeth. 2020; 13:30-6.
16. Bryant C, Jackson H, Ames D. The prevalence of anxiety in older adults: methodological issues and a review of the literature. J Affect Disord. 2008; 109(3):233-250.
17. Wetherell JL, Thorp SR, Patterson TL, Golshan S, Jeste DV, Gatz M. Quality of life in geriatric generalized anxiety disorder: a preliminary investigation. J Psychiatr Res. 2004; 38(3):305.
18. Mantella RC, Butters MA, Amico JA *et al.* Salivary cortisol is associated with diagnosis and severity of late-life generalized anxiety disorder. Psychoneuroendocrinology. 2008; 33(6):773-781.
19. Chaudieu I, Beluche I, Norton J, Boulenger JP, Ritchie K, Ancelin ML. Abnormal reactions to environmental stress in elderly persons with anxiety disorders: evidence from a population study of diurnal cortisol changes. J Affect Disord. 2008; 106(3):307-313.
20. Weber B, Lewicka S, Deuschle M, Colla M, Vecsei P, Heuser. Increased diurnal plasma concentrations of cortisone in depressed patients. Journal of Clinical Endocrinology and Metabolism, 2000, 85.
21. Young EA, Haskett RF, Murphy-Weinberg V, Watson SJ, Akil H. Loss of glucocorticoid fast feedback in depression. Arch Gen Psychiatry. 1991; 48:693-9.
22. Sullivan P, Wilson D, Mulder R, Joyce P. The hypothalamic pituitary–thyroid axis in major depression. Acta Psychiatrica Scandinavica. 1997; 95:370-378.
23. Chakrabarti S. Thyroid Functions and Bipolar Affective Disorder. Journal of Thyroid Research, Article ID 306367, 13 pages, 2011, doi:10.4061/2011/306367
24. Lenze EJ, Mantella RC, Shi P *et al.* Elevated cortisol in older adults with generalized anxiety disorder is reduced by treatment: a placebo-controlled evaluation of escitalopram. Am. J Geriatr. Psychiatry. 2011; 19(5):482-490.
25. Pomara N, Willoughby LM, Sidtis JJ, Cooper TB, Greenblatt DJ. Cortisol response to diazepam: its relationship to age, dose, duration of treatment, and presence of generalized anxiety disorder. Psychopharmacology. 2005; 178(1):1-8.