Role of serum TSH Level in Various Anxiety Disorders in Southern Rajasthan Region of India

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Abstract

Background: Thyroid dysfunctions have been recognized to cause significant manifestations in mental health. They may lead to disturbances in emotions and cognition. Both increase and decrease in thyroid function can cause mood abnormalities. Vice versa, depression can also go hand in hand with subtle thyroid dysfunctions. Psychiatric manifestations usually appear first in cases of hypothyroidism. The aim of this study is to find correlation between serum TSH and patients of generalized anxiety disorder.

Methods: A complete data of all clinically diagnosed cases of generalized anxiety disorder who attended the psychiatric OPD from Nov 2021 to June 2022. A standardized pre-structured questionnaire with consent was filled by direct interview of patients including the demographic and laboratory data.

Results: About 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 with a significant difference. 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. The difference between values of TSH in male cases and control is found statistically significant. In case of females TSH was raised in controls (2.58) than cases (1.79) and difference was found statistically significant.

Conclusions: In our study we found out that there is direct association of serum TSH level with generalized anxiety disorder. We found significantly low levels of serum TSH in generalized anxiety disorder cases.

Keywords: generalized anxiety disorder, TSH, depression, GAD, hypothyroidism

Introduction

Generalized anxiety disorder is characterized by behavioral changes like excessive, uncontrollable and often irrational worry.[1] These behavioral changes are usually interfere with routine activity. An individual with Generalized anxiety disorder concerned about everyday matters such as health issues, interpersonal relationship problems, money, death, family problems, friendship problems or work difficulties.[2] Individuals may exhibit a variety of physical symptoms, including feeling tired, fidgeting, headaches, numbness in hands and feet, muscle tension, difficulty swallowing, upset stomach, vomiting, diarrhea, breathing difficulty, difficulty concentrating, trembling, irritability, sweating, restlessness, sleeping difficulties, hot flashes, rashes, and inability to fully control the anxiety.[3] These symptoms must be consistent and ongoing, persisting at least six months, for a formal diagnosis of GAD.[1]

ICD-10 Generalized anxiety disorder (Chandrashekhar and Reddy, 1998) Note: For children different criteria may be applied. [3]

A period of at least six months with prominent tension, worry, and feelings of apprehension, about everyday events and problems.

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At least four symptoms out of the following list of items must be present, of which at least one from items (1) to (4).

Autonomic arousal symptoms

1. Palpitations or pounding heart, or accelerated heart rate.
2. Sweating.
3. Trembling or shaking.
4. Dry mouth (not due to medication or dehydration).

Symptoms concerning chest and abdomen

1. Difficulty breathing.
2. Feeling of choking.
3. Chest pain or discomfort.
4. Nausea or abdominal distress (e.g. churning in the stomach).

The basolateral complex, medial prefrontal cortex, sensory cortices and the adjacent central nucleus of the amygdale are related with the fear memories. These connections seem less functionally in those with generalized anxiety disorder. Another difference is that the amygdala areas have decreased connectivity with the insula and cingulate areas that control general stimulus salience, while having greater connectivity with the parietal cortex and prefrontal cortex circuits that underlie executive functions. This is consistent with cognitive theories that suggest the use in this disorder of attempts to reduce the involvement of emotions with compensatory cognitive strategies.[4] Receptors for thyroid hormones are located in these areas.

Thyroid dysfunctions can cause abnormal mental health i.e. cognition and emotional disturbances. Hypo or hyper functioning of thyroid may leads to mood disturbance. Vice versa, depression can also go hand in hand with subtle thyroid dysfunctions.[5]

Before prescribing any medication for depression, psychiatrist must ask for evaluation of thyroid function. Even mild cases of hypothyroid state can cause depression.[6,7] One of the most common mistakes which happen is that the concerned doctors fail to look for any psychiatric co morbidity in such patients. Many studies have revealed that there are significantly deranged levels of T3, T4, and thyroid-stimulating hormone (TSH) in patients of depression.[8,9] Mood and anxiety disorders have higher prevalence in patients with thyroid dysfunction.[10] Another study showed a prevalence of depression in 20.5% of the patients of hypothyroidism.[11]

Psychiatric manifestations usually appear first in cases of hypothyroidism. They form about 2–12% of the initial symptoms in about all of the reported cases. Initially, it starts with anxiety, memory lapses, progressive mental slowing, and speech deficits.[12,13] In cases of acute hypothyroidism, anxiety disorders occur in about 30–40% of patients.[14,15] Patients with subclinical hypothyroidism (SCH) can present with anxiety, irritability, poor concentration, slow information processing, and poor learning in comparison to normal subjects.[16,17] Hypothyroidism impacts certain aspects of cognitive functioning and mood. Severe hypothyroidism can cause melancholic depression and dementia, thus causing reduction in health-related quality of life. Although the results are inconsistent, data do suggest that the neuropsychiatric symptoms tend to improve with treatment for both overt hypothyroidism and SCH and normalization to a euthyroid state.[18]

Study of **Maherra Khambathy et al** on cultural aspects of anxiety disorders in India states that the prevalence of generalized anxiety disorder is 5.8%.[19]

The aim of this study is to find correlation between serum TSH and patients of generalized anxiety disorder.

Methods

Study Design - Cross-sectional, Descriptive, Duration Based, Hospital based Study

Place of study – This study was conducted in biochemistry and nephrology department at Pacific Medical College & Hospital, Udaipur (Rajasthan).

Study Population & Inclusion Criteria – Clinically diagnosed cases of generalized anxiety disorder who attended the psychiatric out-patient department during year 2021-2022 which included Southern region of Rajasthan (Udaipur, Chittorgarh, Bhilwara, Rajsamand, Dungarpur, Banswara, Pratapgarh districts).

Study Duration – All criteria defined patients attended from November 2021 to June 2022.

Sample Size – Sample size was calculated by using prevalence of generalized anxiety disorder 5.8%.[19]

$$sample\ size = \frac{z^2 \times p(1-p)}{\text{€}^2}$$

Here **z** is the z score, € is the margin of error, p is the population proportion. By using this formula, minimum 84 subjects have to be included in this study. In our study 105 anxiety diagnosed cases/controls of 15-30 years age were selected attending Psychiatric clinics and rehabilitation clinics and Pacific medical college and hospital, Udaipur, Rajasthan. They were studied under two groups.

GROUP I: - It were consist of healthy control subjects (n=105). Subjects are healthy it was ensure by routine tests. Healthy subjects with no clinical manifestations or history of chronic diseases were included in this group.

GROUP II: - It were consist of subject case (n=105), have symptoms which is diagnosed by psychiatrist.

Data Collection- A standardized pre-structured questionnaire with consent was filled by direct interview of patients. Data was collected regarding demographic detail, marital status, family history and associated medical and surgical conditions.

Ethical issues – Ethical clearance from ethical committee has been obtained prior to beginning of study.

Exlusion Criteria -

1. Subjects below 15 years and above 30 years of age were excluded from the study.

2. Subjects on multivitamins or any supplements, or metabolic disorders and malnutrition were excluded from the study.

3. Hypertensive, Cardiac disease, diabetes, cancer patients are excluded.

4. Systemic disease patients are excluded.

5. Pregnant women are excluded.

Collection and Analysis of Blood Samples - Informed consent has obtained from all subjects for participating in the study. A unique ID number was assigned to each study participant and the same is mentioned on sample container. Under all aseptic precautions, 5 ml of venous blood was drawn from ante-cubital vein and collected in plain sterile vial.

Samples were REMI centrifuged at 3000 RPM for a standard period of 15 minutes at central laboratory of Pacific Medical College and Hospital. Serum were separated after centrifugation. Serum was kept at -20^0C (for cortisol) until assayed.

Estimation of serum TSH: Estimation was done by Electro Chemiluminescence Immunoassay "ECLIA method in Roche Cobas 6000 along with quality control sera for accurate result.

Principle of ECL: Electro Chemi Luminescence (ECL) is Roche's technology for immunoassay detection. Results are reliable on the basis of well-designed, specific and sensitive immunoassays technology. Ruthenium-complex and tripropylamine (TPA) used for development of ECL immunoassays. Electirc voltage is applied to the sample solution resulting in a precisely controlled reaction. ECL technology provides superior performance by accommodating various immunoassay principles.

Statistical Analysis – Done by using excel sheet and statistical software SPSS.

Results

Table 1 show that in our study 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. There was no significance difference found between both groups (p value 0.865). Male participants were 65.7% whereas 34.2 % were females. Table also depicted that 48.57% of cases were observed to be married while 51.42 % were unmarried with no significant difference (p value 0.543) among cases and controls. Study findings show that 48.5% of cases complained of reduced appetite while in control subjects appetite was good in 71.4% of individuals. There was no significant difference between type of Appetite in cases and control (p value 0.201). About 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 with a significant difference (p value 0.027 which is less than 0.05). (Table 1)

Table 2 shows that there is significant difference (P 0.041) in pulse between cases (82.53±6.82) and control (88.31±10.13). The table also shows that mean systolic BP of cases is 116.32±8.9 and while in control mean systolic BP is 118.2±8.3. There is no significant difference in systolic blood pressure between cases and control. Similarly, mean diastolic BP of cases is 73.27±3.1and while in control mean diastolic BP is 77.73±6.87.There is no significant difference in diastolic blood pressure between cases and control. 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). (Table 2)

Table 3 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). (Table 3).

Table No. 1 Demographic distribution of cases and control

S. No.	Variables	Cases (n= 105)		Control (n= 105)	
		N	%	n	%
Age group					
1.	15-20 yr	24	22.8	27	25.7
2.	20-25yr	33	31.4	24	22.8
3.	25-30 Yr	48	45.7	54	51.4
Sex					
1.	**Male**	69	65.7	60	57.14
2.	**Female**	36	34.2	45	42.85
Marital Status					
1.	**Married**	51	48.57	60	57.14
2.	**Unmarried**	54	51.42	45	42.85
Appetite					
1.	**Good**	54	51.4	75	71.4

2.	**Decreased**	51	48.5	30	28.5
Family History					
1.	**Yes**	54	51.4	27	25.7
2.	**No**	51	48.5	78	74.2

Table 2 Mean ±SD Values of Pulse, systolic, diastolic blood pressure and TSH level in case and control

Variables	Case	Control	Total	P value
Pulse	82.53±6.82	88.31±10.13	85.42±8.35	0.041
SBP	116.32±8.9	118.2±8.3	117.26±5.33	0.431
DBP	73.27±3.1	77.73±5.5	75.5±2.09	0.062
TSH	1.32±0.32	2.48±0.99	1.90±1.24	0.0001

Table 3. Gender wise Mean ±SD Values of TSH in case and control.

TSH	Case	Control	Total	P Value
Male	1.31±0.24	2.46±0.87	1.88±0.95	0.001
Female	1.79±0.99	2.58±0.94	2.18±0.87	0.019

Discussion

In our study – Significant difference has been observed in family history of similar illness among cases and control. (p value 0.027 which is less than 0.05)

Our study also shows that there is significant difference (p value is 0.041) in pulse rate between cases and control, mean value (82.53±6.82) and (88.31±10.13) respectively. However there were no significant difference in systolic and diastolic blood pressure between cases and control. There was significant difference between mean values of TSH in case and control (p value =0.001) which established the role of serum TSH level in cases of generalized anxiety disorder.

The significant difference between values of serum TSH in male cases and control (p value = 0.001) as well as female cases and controls (p<0.019).

Chaudhary et al (2020) 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. [20]

Generalized Anxiety Disorder (GAD) is a common and impairing anxiety disorder in older adults (Bryant et al., 2008[21]; Wetherell et al., 2004[22]), and it has been associated with elevated cortisol in this age group (Mantella et al., 2008[23]; Chaudieu et al., 2008[24]).

Summary & Conclusion

In our study we found out that there is direct association of serum TSH level with generalized anxiety disorder.

Anxiety disorders are a cluster of mental disorders characterized by significant and uncontrollable feelings of anxiety and fear[6] such that a person's social, occupational, and personal function are significantly impaired.[6] Anxiety may cause physical and cognitive symptoms, such as restlessness, irritability, easy fatiguability, difficulty concentrating, increased heart rate, chest pain, abdominal pain, and a variety of other symptoms that may vary based on the individual.[6]

The interpretation of these data is difficult because analysis of many studies demonstrate that not all patients with generalized anxiety disorder have hypothyroidism, and not all patients with hypothyroidism have generalized anxiety disorder.

So to conclude we can say that most of our Study individuals 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 generalized anxiety disorder. But only family history was found statistically significantly related. Serum TSH was measured and we found significantly low levels of serum TSH in generalized anxiety disorder cases.

Limitations

The data was taken only from hospitalized patients. This study was conducted on a small population group with limited resources and financial restrictions.

References

1. Association, American Psychiatric (2013). Diagnostic and statistical manual of mental disorders : DSM-5 (5th ed.). Washington, D.C.: American Psychiatric Association. p. 222. ISBN 978-0-89042-554-1.

2. Torpy, Janet M.; Burke, AE; Golub, RM (2011). "Generalized Anxiety Disorder". JAMA. 305 (5): 522. doi:10.1001/jama.305.5.522. PMID 21285432.

3. The ICD-10 Classification of Mental and Behavioural Disorders available at http://www.who.int/classifications/icd/en/bluebook.pdf pg24-31 acessed on 2-07-2022

4. *Möller, Hans-Jürgen; Bandelow, Borwin; Bauer, Michael; Hampel, Harald; Herpertz, Sabine C.; Soyka, Michael; Barnikol, Utako B.; Lista, Simone; Severus, Emanuel; Maier, Wolfgang (26 August 2014). "DSM-5 reviewed from different angles: goal attainment, rationality, use of evidence, consequences—part 2: bipolar disorders, schizophrenia-spectrum disorders, anxiety disorders, obsessive–compulsive disorders, trauma- and stressor-related disorders, personality disorders, substance-related and addictive disorders, neurocognitive disorders". European Archives of Psychiatry and Clinical Neuroscience. 265 (2): 87–106.*doi:10.1007/s00406-014-0521-9. PMID 25155875.

5. Depression and Other Common Mental Disorders: Global Health Estimates. Geneva: World Health Organization; 2017. Licence: CC BY-NC-SA 3.0 IGO.

6. Kessler RC, McGonagle KA, Zhao S, et al. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States. Results from the National Comorbidity Survey. Arch Gen Psychiatry. 1994;51(1):8- 19.

7. Borwin Bandelow and Sophie Michaelis, Epidemiology of anxiety disorders in the 21st century, Dialogues in Clinical Neuroscience - Vol 17 . No. 3 . 2015

8. Available at http://ghana.westafrican-rescue.com/Files/anxiety-disorders-pdf.aspx. S.D. Attu. accessed on 22-04-2018

9. Available at https://www.nhp.gov.in/Anxiety-Disorders_mtl: National Health Portal. accessed on 22-04-2018

10. Available at http://www.healthcollective.in/2017/07/long-read-anxiety-disorders-in-india/ accessed on 22-04-2018.

11. Walker JJ, Terry JR, Lightman SL. Origin of ultradian pulsatility in the hypothalamic–

pituitary–adrenal axis. Proc. Biol. Sci. 277(1688), 1627–1633 (2010).

12. Strohle A, Holsboer F. Stress responsive neurohormones in depression and anxiety. Pharmacopsychiatry 36(Suppl. 3), S207–S214 (2003).

13. Chrousos GP, Gold PW. The concepts of stress and stress system disorders. Overview of physical and behavioral homeostasis. JAMA 267(9), 1244–1252 (1992).

14. Holsboer F. Psychiatric implications of altered limbic-hypothalamic–pituitary–adrenocortical activity. Eur. Arch. Psychiatry Neurol. Sci. 238(5–6), 302–322 (1989).

15. Heim C, Ehlert U, Hellhammer DH. The potential role of hypocortisolism in the pathophysiology of stress-related bodily disorders. Psychoneuroendocrinology 25(1), 1–35 (2000).

16. Vreeburg, S.A., Zitman, F.G., van Pelt, J., Derijk, R.H., Verhagen, J.C., van Dyck, R., Hoogendijk, W.J., Smit, J.H., Penninx, B.W., 2010. Salivary cortisol levelsin persons with and without different anxiety disorders. Psychosom. Med. 72, 340—347.

17. Désir, D., Van Cauter, E., Golstein, J., Fang, V.S., Leclercq, R., Refetoff, S., & Copinschi, G. (1980). Circadian and ultradian variations of ACTH and cortisol secretion. Hormone Research, 13, 302–316.

18. Kirschbaum, C., & Hellhammer, D.H. (2000). Salivary cortisol. In G. Fink, (Ed.),

Encyclopedia of stress (pp. 379–383). San Diego: Academic Press.

19. Maherra Khambaty et al. Cultural aspects of anxiety disorders in India. Dialogues Clin Neurosci. 2017 Jun; 19(2): 117–126. doi: 10.31887/DCNS.2017.19.2/rparikh

20. Chaudhary R, Chabra S, Singla M, Mishra BP, Sharma A. Psychiatric morbidity among hypothyroid patients – A hospital based study. Delhi Psychiatry J 2014; 17:35-8.

21. 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 Aug; 109(3):233–250.

22. 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 May-Jun; 38(3):305–312.

23. Mantella RC, Butters MA, Amico JA, et al. Salivary cortisol is associated with diagnosis and severity of late-life generalized anxiety disorder. Psychoneuroendocrinology 2008 Jul; 33(6):773–781.

24. 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 Mar; 106(3):307–313.