

Thyroid Dysfunction and its Effect on Quality of Life in Patients of Anxiety Disorders

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Received: 14-01-2023 / Revised: 17-02-2023 / Accepted: 13-03-2023

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Conflict of interest: Nil

Abstract

Objective: To study thyroid dysfunction and its effect on quality of life in patients of anxiety disorders.

Methods: A cross sectional study in total 90 patients diagnosed with Anxiety disorders as per ICD 10 after applying inclusion criteria and taking informed consent were included in the study. Data was analysed keeping in view the aims and objectives of the study.

Results: The results of the present study indicated higher levels of anxiety in patients with hypothyroidism. Most of the patients belonged to the 18–30 years of age group, female preponderance, educated till primary school, belong to upper lower and lower class of the society and resided in rural areas. Domains 1, 2, & 4 of WHOQOL BREF were found to be significantly associated with Anxiety disorder with hypothyroidism in comparison to Anxiety disorder alone or Anxiety disorder with hyperthyroidism. Mean anxiety score for hypothyroidism was found to be higher as compared to euthyroidism and hyperthyroidism and this difference in mean anxiety scores was found to be statistically significant.

Conclusion: Holding educational programs and protocols about thyroid disease to improve the mental health is suggested. Results indicated the relationship between anxiety, thyroid disorders and quality of life; therefore, it is necessary to pay attention to their importance in such patient's care and treatment programs design. The present study suggested the usefulness of a longitudinal study exploring the temporal correlation between anxiety and thyroid disorders, as it could shed further light on this topic.

Keywords: Hamilton Anxiety Rating Scale (HAM-A), Anxiety Symptoms, World Health Organization Brief Quality Of Life Questionnaire (WHOQOL-BREF).

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Introduction

Anxiety Disorder: Among the psychiatric morbidities, Anxiety disorders are the most prevalent and sixth leading cause of disability worldwide with 4% of all YLD (years lived with disability). Females are more commonly affected than males. In India as per the National Mental Health Survey 2015-16, 2.57% was the prevalence of Anxiety disorder, among anxiety disorder, Agoraphobia was the most common with prevalence of 1.6% followed by Generalised anxiety disorder was 0.57% prevalence [1,2]. An Anxiety disorder may make the person feel anxious most of the time, without any apparent reason. The exact cause of anxiety disorders is unknown. It may be either inherited or acquired [3].

Quality of life Quality of life has been defined by the World health Organization as “individuals perception of their position in life in the context of the culture and value systems in which they live, and in relations to their goals, expectations, standards and concerns” [4].

Till date, no tool is available to accurately measure human sufferings. One of the many approaches to this difficult yet invaluable task the concept of “Quality of life” has been evolved. This concept firstly developed in the social sciences and later on applied in medical practice to determine if available cancer treatments could not only increase the survival time of patients but also improve their sense of well-being.

According to Patrick and Erickson, life has two dimensions: quantity and quality. Quantity of life is expressed in terms of “hard” biomedical data, such as mortality rates or life expectancy. Quality of life refers to complex aspects of life that cannot be expressed by using only quantifiable indicators; it describes an ultimately subjective evaluation of life in general. It encompasses, though, not only the subjective sense of well-being but also objective indicators such as health status

and external life situations. Data about quality of life can be used to estimate the impact of different diseases on functioning and well-being, to compare outcomes between different treatment modalities (such as medication and surgery) and to differentiate between two therapies with marginal differences in mortality and/or morbidity [5–7]. During the past several decades, there has been an increasing focus on quality-of-life issues and outcomes in anxiety disorder. This has been aided by the development of World Health Organization quality-of-life (WHOQOL) instruments to assess Quality of life.

Thyroid Abnormalities Thyroid hormones are essential for normal development and growth of many target tissues, including the brain and the skeleton. Thyroid hormone action on critical genes for neurodevelopment is limited to specific time window, and even a short period of deficiency of thyroid hormone (TH) can cause irreversible brain damage. The association between Thyroid function and Psychiatric disorders particularly mood disorders has long been recognized.

Today, it is well recognized that thyroid dysfunction may significantly affect mental status including emotion and cognition. Both excess and insufficient thyroid hormones can cause mood abnormalities including depression and anxiety that is generally reversible with adequate thyroid treatment. Hypothyroidism and hyperthyroidism are found to be associated with increased susceptibility to anxiety which leads to decrease in QOL. Regular treatment of hypothyroidism and hyperthyroidism with restoration of euthyroidism may not fully restore QOL even after many years, indicating that such patients have difficulties adapting to and coping with their illness, thus experiencing marked and longstanding limitations in

physical, mental and psychosocial functioning [8,9]

Anxiety and Thyroid dysfunction have a significant and negative impact on quality of life independently. However less is known about the effects of Thyroid dysfunction on Quality of life in patients of Anxiety disorders.

Hence the current study was conceptualized to study quality of life and thyroid abnormalities among patients with Anxiety disorder. By understanding the severity of anxiety and its relationship with stressful life events, quality of life and the management of illness can be focused, so that psychiatric and medical morbidity can be reduced.

Materials and Methods

Present study was a cross sectional study conducted at Department of Psychiatry, Chirayu Medical College and Hospital, Bhopal with the aim to determine thyroid dysfunction and its effect on quality of life in patients of Anxiety disorders. In total 90 patients diagnosed with Anxiety disorders as per ICD 10 after applying inclusion criteria and taking informed consent were included in the study. Data was analysed keeping in view the aims and objectives of the study

Study Design: Cross Sectional Study

Study Site: Department of Psychiatry, Chirayu Medical College and Hospital, Bhopal

Study Duration: One and half year (1 January 2021-30 June 2022)

Study Population: Patients diagnosed with Anxiety disorder as per ICD 10 were included in the study.

Sample Size: 90

Inclusion Criteria:

- Patients having Anxiety disorder diagnosed according to ICD-10 criteria.
- Patients between 18-60 yr of age of either sex

- Patient who gave informed as well as written consent.

Exclusion Criteria:

- Patients known to have any medical co-morbidity other than thyroid dysfunction.
- Patients having any psychiatric illness other than Anxiety disorder
- Patients with a history of substance dependence.
- Pregnant and lactating women.

Consent-Informed consent was taken as per the standard procedure in the institution.

Ethical clearance-It was obtained from the Ethical Committee of Chirayu Medical College & Hospital Bhopal.

Method of data collection-

- Permission from the institutional ethics committee and university clearance was obtained.
- Meeting and rapport building with the study participants.
- The study subjects diagnosed with Anxiety disorder were included in this study.
- The patients were provided with the study information sheet and consent form and were explained about the relevant details about the study in a language best understood by them.

Informed written consent was obtained after explaining about the purpose, nature and process of the study and then data collection was started.

Tools/Instruments used-

- **Semi-structured proforma-** To assess the socio-demographic variables of the patients.
- **International classification of mental and behavioural disorders - 10th revision,** version clinical description an diagnostic guidelines (ICD-10) for diagnosing Anxiety disorder.
- **Hamilton Anxiety Rating Scale** was used to assess the severity of anxiety.

The HAM-A was one of the first anxiety rating scale developed in 1959 by Dr. M. Hamilton to measure the severity of anxiety symptoms. The HAM-A probes 14 parameters, Each item is scored on a 5-point scale, ranging from 0=not present, 1=mild, 2=moderate, 3=severe, 4=very severe.

Thyroid profile- Among all the patients with Anxiety disorder, detailed clinical examination and assessment T3, T4 and TSH was done.

- The blood sample was drawn in the fasting state between 9 am to 10 am and triiodothyronine (T3), thyroxin (T4), and thyroid stimulating hormone (TSH), was estimated using ECLIA (Electro-Chemiluminescence Immunoassay) using machine **COBAS Roche e411**.
- On the basis of assessment, patients were divided into Euthyroid,

Hyperthyroid and Hypothyroid (clinical + subclinical).

WHOQOL-BREF Scale- After that in all patients WHOQOL-BREF (World Health Organizations Quality of Life) Scale was applied to assess the quality of life. WHOQOL-BREF captures many subjective aspects of quality of life. It is one of the best known instruments that has been developed for cross-cultural comparisons of quality of life and is available in more than 40 languages. It is a **26-item** instrument consisting of **four domains**:

- Physical health
- Psychological health
- Social relationships
- Environmental health

Each individual item of the WHOQOL-BREF is scored from 1 to 5 scale, the scores are then transformed linearly to a 0–100 scale.

Observation Chart

Table 1: Distribution of patients according To age group

Age Group	Frequency	Percentage
18-30 years	42	46.7%
31-40 years	35	38.9%
41-50 years	7	7.8%
51-60 years	6	6.7%

Most of the patients belonged to the 18 – 30 years of age group (46.7%), 38.9% of patients belonged to age group of 31 – 40 years, 7.8 % of patients belonged to age group of 41 – 50 years and least number of patients; 6.7% belonged to 51 – 60 years of age group.

Table 2: Distribution of patients according to gender

Gender	Frequency	Percentage
Male	39	43.3%
Female	51	56.7%

In this study, 56.7% of patients were females and 43.3% were males

Table 3: Distribution of patients according to education

Education	Frequency	Percentage
Illiterate	5	5.6%
Primary School	23	25.6%
Middle School	16	17.8%
High School	16	17.8%
Higher Secondary School	15	16.7%
Graduate and Above	15	16.7%

In this study, 25.6% of patients were educated up to primary school and 5.6 % were illiterate.

Table 4: Distribution according to hamilton anxiety rating scale

Hamilton Anxiety Rating Scale (HAM-A)	Frequency	Percentage
0-17 (Mild)	7	7.8%
18-24 (Mild to Moderate)	51	56.7%
25-30 (Moderate to Severe)	31	34.4%
>30 (Severe)	1	1.1%

Table 5: Distribution according to whoqol - bref

WHOQOL - BREF Raw Score	Mean	Standard Deviation	Minimum	Maximum
Physical Health	19	3	11	23
Psychological Health	16	3	10	21
Social Relationship	11	2	6	14
Environment	23	3	16	33
Total WHOQOL - BREF Score	75	6	58	89

Mean score of total WHOQOL - BREF score was 75 ± 6 . Domain physical health, mean score was 19 ± 3 . Domain psychological health, mean score was 16 ± 3 . Domain Social Relationship, mean score was 11 ± 2 . Domain environmental health, mean score was 23 ± 3 .

Table 6: Thyroid dysfunction and ham-a wise distribution

Thyroid dysfunction	Hamilton Anxiety Rating Scale (HAM-A)				Total	Chi-square	p Value
	0-17 (Mild severity)	18-24 (Mild to Moderate Severity)	25-30 (Moderate to Severe)	>30 (Severe)			
	N (%)	N (%)	N (%)	N (%)			
Hypothyroid (clinical + Subclinical)	0 (0%)	4 (7.8%)	5 (16.1%)	0 (%)	9(10%)	23.733	0.001*
Euthyroid	7(100%)	18(35.3%)	3(9.7%)	0(0%)	28(31.1%)		
Hyperthyroid	0(0%)	29(56.9%)	23(74.2%)	1(100%)	53(58.9%)		
Total	7(100%)	51(100%)	31(100%)	1(100%)	90(100%)		

Chi Square test* $p < 0.05$

Table 7 Mean comparison between thyroid dysfunction with Ham-a score and whoqol - bref.

	Hypothyroid	Euthyroid	Hyperthyroid	Total	F	p Value
	Mean \pm S.D.	Mean \pm S.D.	Mean \pm S.D.	Mean \pm S.D.		
HAM-A	24.9 \pm 2.8	21.2 \pm 3.5	24.5 \pm 3.1	23.5 \pm 3.5	11.133	.000
Physical Health	17.4 \pm 1.7	20.3 \pm 1.9	17.9 \pm 2.5	18.6 \pm 2.5	11.199	.000
Psychological Health	13.8 \pm 3	18.4 \pm 1.6	15.5 \pm 2.2	16.2 \pm 2.6	24.231	.000
Social Relationship	10 \pm 2.1	11.1 \pm 1.7	10.3 \pm 1.7	10.5 \pm 1.8	2.172	.120
Environment	23 \pm 3.3	25 \pm 3.3	22 \pm 2.8	90 \pm 23	9.034	.000

Statistical Analysis:

Data was collected and entered simultaneously in Statistical Package for Social Sciences (SPSS) version 23 and coded appropriately. The data was analysed keeping in view the aim and objectives of the study. Descriptive analysis was used to summarize the data for a group. This process helps in understanding the specific set of observations. In this study under descriptive analysis frequency and percentage of age group, gender and education of study participants were used and were compared against categories of HAM-A Scale. Graphs and Charts were made. Chi square test was used to compare HAM-A Scale and Thyroid dysfunction, ANOVA Test was applied to compare the means of HAM-A score, WHOQOL against Thyroid dysfunction. Significance was set at standard 0.05.

Results

1. Most of the patients belonged to the 18 – 30 years of age group. Majority of the study participants were females.
2. Majority of the study participants were educated till primary school and belonged to upper lower and lower class of the society and resided in rural areas. Majority of the study participants had mild to moderate anxiety followed by moderate to severe anxiety.
3. According to WHOQOL-BREF, maximum mean score was observed for environment domain and least for social relationship domain. Majority of the patients with mild anxiety were males with mild to moderate and moderate to severe anxiety were females. Majority of the subjects were found to have raised T3, T4 and normal TSH levels. Majority of the subjects were hyperthyroidism.
4. Mean anxiety score for hypothyroidism was found to be higher as compared to euthyroidism and hyperthyroidism and this difference in mean anxiety scores was found to be statistically significant.
5. Domains 1, 2, & 4 of WHOQOL BREF were found to be significantly associated with Anxiety disorder with hypothyroidism in comparison to Anxiety disorder alone or Anxiety disorder with hyperthyroidism.

Discussion

Socio-demographic characteristics: In present study, mean age of the study participants was 32 ± 11 years ranging from 18 – 65 years. Majority of the study participants were in the age group of 18-30 years (46.7%) followed by 38.9% in the age group of 31-40 years. Female preponderance was seen, 56.7% were females and 43.3% were males. Binu et al in their study reported mean age of 38.09 ± 12.67 years and majority of the study participants were in the age group of 20-39 years. Also, 79% were females and 20% were males. Similar results were reported by Bukvic et al. Larger proportion of the study subjects were educated up to primary school (25.6%) and 5.6% were illiterate. Majority of the patients in this study were residing in rural areas and belonged to upper lower followed by lower class of the society. Majority of the patients with mild anxiety were educated up to higher secondary class, patients with mild to moderate anxiety were educated up to primary class, patients with moderate to severe anxiety were educated up to higher secondary class and the patient with severe anxiety was graduate. Bukvic et al in their study reported majority of the study participants were average earning and educated till primary school. Binu et al in their study reported majority of the study participants were literate (76%) and belonged to middle class. The higher prevalence in lower economic class supports the similar finding by Branka et al. [10]

Type of anxiety-It was found that generalized anxiety disorder 36.7% was the most commonly found disorder, followed by panic disorder 26.7%, Agoraphobia without panic disorder was

the least found disorder 4.4%. Sheikh et al in their study reported that, generalized anxiety was present in 6.25% of the study participants, 2.34% had depressive disorders, 1.56% had panic disorders, 0.78% had phobia and OCD each. Mohapatra et al in their study reported that 42 (2.86%) patients had different anxiety disorders; out of which 16 (38.1%) patients had obsessive compulsive disorder, 10 (23.81%) patients had specific phobias, 6 (14.29%) patients had generalized anxiety disorder, 4 (9.52%) patients had social anxiety disorder and 3 (7.14%) patients each had separation anxiety disorder and panic disorder. [11-13]

Hamilton Anxiety rating scale and socio demographic characteristics: In present study, it was found that majority of the study participants had mild to moderate anxiety (56.7%) followed by moderate to severe anxiety (34.4%). 7.8% had mild anxiety and 1.1% had severe anxiety. Bathla et al in their study reported 29% had mild anxiety, 14% had moderate anxiety, 9% had severe anxiety and 9% had very severe anxiety. [14] Among all patients with anxiety, majority of the study participants with mild to moderate anxiety (42.9%) and moderate to severe anxiety (49%) were in the age group of 18-30 years. Only one patient had severe anxiety that belonged to 18 – 30 years of age. Although majority of the patients in this study were females, majority of the study participants with mild (57%) and severe (100%) anxiety were males. Patients with mild-moderate (58.8%) and moderate-severe (58.1%) anxiety were females. Similar results were reported by Bathla et al, that higher number of patients categorized under mild and moderate Anxiety were males which is in line with our findings. Majority of the patients in this study reside in rural area. In present study, patients with mild anxiety were belonging to urban residential area (57.1%), with mild to moderate (51%) and moderate to severe anxiety (54.8%) belonging to rural residential area, and one

patient with severe anxiety was from urban area. [15,16]

Thyroid abnormalities and Anxiety disorders: Majority of the subjects were hyperthyroid (58.9%). Total 10% of patients were hypothyroid. 31.1% were euthyroid. [17] Those who were hyperthyroid, majority had mild to moderate anxiety followed by moderate to severe anxiety and severe anxiety. Association between Thyroid dysfunction and HAM-A scale was found to be statistically significant. Mehnaz et al in their study reported that hypothyroid patients have significant differences in all aspects of mental health compared with the normal people. [18] It was revealed that these patients have the highest severity of depression, physical signs and Anxiety. Shoib et al in their study reported participants with hyperthyroidism and euthyroidism showed Hamilton Anxiety Scale (HAM-A) scores of 27.1 and 15.5, respectively. [19]

Emotional and behavioural problems can be manifested due to underlying medical cause like endocrinal, cardiac, neurological, immunological, gastroenterological or other chronic medical diseases. Stress, malnutrition, smoking, circadian variation, sleep deprivation, pregnancy, ageing, thyroid medications, other medications (lithium, corticosteroids, phenytoin, salicylates, furosemide, propranolol, amiodarone) and concurrent clinical disease are just a few of the factors that affect thyroid hormone levels. This greatly complicates the designs of any thyroid hormone studies that might be conducted. Although it is obvious that thyroid dysfunction is not the cause of anxiety and that patients are generally considered to be euthyroid, many Anxiety disorder patients exhibit minor changes in thyroid function as a result of altered hypothalamus-pituitary-thyroid axis (HPT) activity. [20]

Anxiety disorders and quality of life: In present study quality of life scores progressively decreased as severity of

anxiety increased. Bukvic et al in their study reported that mood/behaviour disturbances, depression and anxiety, correlated significantly with decreased QOL and not only with the mental aspect of QOL, but also with the physical aspect of QOL. Mauro et al in their study reported that anxiety disorders as illnesses that markedly compromise quality of life and psychosocial functioning. Significant impairment can also be found in individuals with subthreshold forms of anxiety disorder. Thus, the medical professional need to communicate with patient about the impact of their level of depression and anxiety on QOL and wellbeing in order to increase motivation and enhance their confidence to receive and maintain their treatment course. [21]

Correlation between Anxiety disorders, Quality of life and Thyroid abnormalities:

Mean anxiety score for hypothyroidism (24.9 ± 2.8) was found to be higher as compared to euthyroidism (21.2 ± 3.5) and hyperthyroidism (24.5 ± 3.1) and this difference in mean Anxiety scores was found to be statistically significant. Eva-Maria Siegmann et al in their study reported chance of developing anxiety disorders is more than 2 times higher among patients with hypothyroidism compared with healthy controls. Mehnaz et al in their study reported mean anxiety scores of 16.34 ± 3.72 in hypothyroidism patients. [22]

Also mean quality of life scores were lower for hypothyroidism as compared to Euthyroidism or hyperthyroidism. In contrast to our findings, Mahnaz et al in their study reported the quality of life of patients with hypothyroidism and normal people was the same, although the physical signs, Anxiety and depression were higher and more severe in the hypothyroid group. This variation might result from the diversity of the study population, the study population's culture, or the type of investigation method. In this regard, the findings of a review study on analysing the

instruments used to assess the symptoms, state of health, and quality of life of hypothyroid patients revealed that many of the methods used were insufficient for the investigations' goals, which could increase or change the findings.

Mehnaz et al in their study also reported significant correlation between anxiety scores with hypothyroidism and QOL with hypothyroidism. In present study it was found that Domain 1, 2, 3, & 4 of WHO-QOL BREF were significantly associated with anxiety disorder with hypothyroidism in comparison to Anxiety disorder alone or Anxiety disorder with hyperthyroidism. This suggests that, compared to anxiety disorder alone, anxiety disorder co-morbid with thyroid abnormalities has a considerable influence on physical, psychological, social relationships, and environmental domains of quality of life. This can be explained by comparing the clinical experiences of thyroid abnormalities and anxiety disorders, which can both include psychological and physical symptoms that have a detrimental effect on a person's quality of life.

Conclusion

Regarding results of the present study indicating higher levels of anxiety in patients with hypothyroidism, holding educational programs and protocols about this disease to improve the mental health is suggested. Also, these results indicate the relationship between anxiety, thyroid disorders, and quality of life; therefore, it is necessary to pay attention to their importance in such patient's care and treatment programs design. Still, the present study suggests the usefulness of a longitudinal study exploring the temporal correlation between anxiety and thyroid disorders, as it could shed further light into this topic. Moreover, further epidemiological studies are necessary to gauge the degree of the problem. Therefore, the implementation of a routine screening for mental illness would prove further useful in facilitating a better outcome.

Declarations**Funding:** None**Conflicts of interest/Competing interests:** None**Availability of data and material:** Department of Psychiatry, Chirayu Medical College and Hospital, Bhopal**Code availability:** Not applicable.**Consent to participate:** Consent taken.**Ethical Consideration:** There are no ethical conflicts related to this study.**Consent for publication:** Consent taken.**Strengths:**

1. As the study was conducted under routine programmatic settings, the finding reflects the ground reality and provide actionable information.
2. The study was unbiased as a single researcher who is not a service provider has carried it out independently. The study used standardized research diagnostic criteria and valid tools for assessment.

Limitation:

1. As the present study was conducted in a medical college hospital, the result observed are subject to bias arising from rate of reporting at the hospital.
2. In order to increase the extension capability of these findings, the population and sample size must be larger and multiple.
3. Causal pathways underlying the reported associations cannot be ascertained, also anxiety overtime could not be measured as it was a cross sectional study
4. Over reporting is a well-recognized issue for self-report surveys.
5. Various factors which could not be taken care of during the study were medications like antithyroid drugs, other medications which can lead to anxiety, any on-going psychosocial stressors and coping skills.

References

1. Murthy RS. National mental health survey of India 2015–2016. *Indian journal of psychiatry*. 2017 Jan;59(1):21.
2. Zahid MF, Haque A, Aslam M, Aleem NA, Hussain S, Fahad H, Naqvi HA, Ghias K. Health-related anxiety and hypochondriacal concerns in medical students: A cross-sectional study from Pakistan. *Teaching and learning in medicine*. 2016 Jul 2;28(3):252-9.
3. MW. P. Definitions of quality of life: what has happened and how to move on. *Top Spinal Cord Inj Rehabil*. 20(3):167–80.
4. Dolan P. The measurement of health-related quality of life for use in resource allocation decisions in health care. *Handbook of health economics*. 2000 Jan 1;1:1723-60.
5. Dimenas ES, Dahlof CG, Jern SC WI. Defining quality of life in medicine. *Scand J Prim Heal Care Suppl*. 1990; 1:7–10.
6. B S. Introduction, in *Quality of Life and Pharmacoeconomics in Clinical Trials*. In: Edited by Spilker B. Philadelphia L-R, Editor. 1996; 1–10.
7. Shoib S, Ahmad J, Wani MA, Ullah I, Tarfarosh SF, Masoodi SR, Ramalho R. Depression and anxiety among hyperthyroid female patients and impact of treatment. *Middle East Current Psychiatry*. 2021 Dec;28(1):1-6.
8. Vita R, Caputo A, Quattropiani MC, Watt T, Feldt-Rasmussen U, Puleio P, Benvenga S, Martino G. Quality of life in patients with hyperthyroidism: where do we stand? *Mediterranean Journal of Clinical Psychology*. 2020 Aug 13;8(2).
9. Yatham LN, Kennedy SH, Parikh S V, Schaffer A, Bond DJ, Frey BN, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 guidelines for the management of patients with bipolar

- disorder. *Bipolar Disord.* 2018; 20(2): 97–170.
10. Freitas J. Development and validation of in vitro bioassays for thyroid hormone receptor mediated endocrine disruption. Wageningen University and Research; 2012.
 11. Vickers AE, Heale J, Sinclair JR, Morris S, Rowe JM, Fisher RL. Thyroid organotypic rat and human cultures used to investigate drug effects on thyroid function, hormone synthesis and release pathways. *Toxicology and applied pharmacology.* 2012 Apr 1; 260(1):81-8.
 12. Belmaker RH, Agam G. Major depressive disorder. *N Engl J Med.* 2008;358(1):55–68.
 13. Atterwill CK, Bunn SJ, Atkinson DJ, Smith SL, Heal DJ. Effects of thyroid status on presynaptic alpha 2-adrenoceptor function and beta-adrenoceptor binding in the rat brain. *J Neural Transm.* 1984;59(1):43–55.
 14. Bathla M, Singh M, Relan P. Prevalence of anxiety and depressive symptoms among patients with hypothyroidism. *Indian J Endocrinol Metab.* 2016;20(4):468–74.
 15. Hall RC, Hall RC. Anxiety and endocrine disease. *Semin Clin Neuropsychiatry.* 1999;4(2):72–83.
 16. Haggerty JJJ, Garbutt JC, Evans DL, Golden RN, Pedersen C, Simon JS, et al. Subclinical hypothyroidism: a review of neuropsychiatric aspects. *Int J Psychiatry Med.* 1990;20(2):193–208.
 17. Davis JD, Tremont G. Neuropsychiatric aspects of hypothyroidism and treatment reversibility. *Minerva Endocrinol.* 2007;32(1):49–65.
 18. Gorkhali B, Sharma S, Amatya M, Acharya D, Sharma M. Anxiety and Depression among Patients with Thyroid Function Disorders. *J Nepal Health Res Counc.* 2020;18(3):373–8.
 19. Branka B, Sandra S, Dejana S, Ivan P, Aleksandar D, Katarina T, et al. Quality of life, anxiety and depression in patients with thyroid diseases and correlating factors. *Acta Medica Mediterr.* 2014;30(3):731–6.
 20. Satyakam Mohapatra, Vivek Agarwal, Prabhat Sitholey AA. A clinical study of anxiety disorders in children and adolescents from North Indian children and adolescents clinic. *Asian J Psychiatry.* 2014;8:84–8.
 21. Rakhshan M, Ghanbari A, Rahimi A, Mostafavi I. A comparison between the quality of life and mental health of patients with hypothyroidism and normal people referred to motahari clinic of Shiraz university of medical sciences. *Int J Community Based Nurs Midwifery.* 2017;5(1):30–7.
 22. Mendlowicz MV, Stein MB. Quality of life in individuals with anxiety disorders. *American Journal of Psychiatry.* 2000 May 1;157(5):669-82.
 23. Dheyab Z. S. Clinically Important Yersinia: Minireview . *Journal of Medical Research and Health Sciences.* 2022; 5(10): 2295–2306.