Open Access

Pak J Med Res
Vol. 61, No. 2, 2022

Original Article

Clinical Spectrum of Thyroid Disorders; An Experience at a Tertiary Care Hospital in Peshawar

Faheem Ullah, Sobia Sabir Ali, Hira Tahir
Department of Diabetes & Endocrinology, MTI, Lady Reading Hospital, Peshawar.

Abstract

Objective: The present study was conducted to explore the different clinical presentations of thyroid disorders among the patients presenting at the Endocrinology Clinic at Medical Teaching Institution (MTI) Lady Reading Hospital.
Study type, settings & duration: A cross-sectional study was conducted at the Department of Diabetes & Endocrinology, Medical Teaching Institution (MTI), Lady Reading Hospital, Peshawar from January to July 2021.
Methodology: The sample of 66 subjects to screen for thyroid disorders. Patients' demographic data, clinical, biochemical and thyroid symptomatology profile was collected using a pre-structured questionnaire.
Results: Most of the patients were found to have hyperthyroidism (72.7%), followed by hypothyroidism (12.1%), subclinical hypothyroidism (9.1%) and subclinical hyperthyroidism (6.1%). The most common symptoms observed among hypothyroid patients were weight gain and cold intolerance (87.5% each), while weight loss and heat intolerance were prominent among hyperthyroid patients, i.e. 97.9% and 93.8%, respectively. Anxiety was most common among the neuropsychiatric symptoms (81.8% overall), reported by all patients with hyperthyroidism and subclinical hyperthyroidism, while 12.5% and 16.7% of patients with hypo and subclinical hypothyroidism reported so. Thyroid swelling was detected among all patients (98.5%), irrespective of under or overactive thyroid. Based on the diagnostic test, anti-thyroid peroxidase (TPO) was present among 4.54% of patients, while thyroid receptor antibody (TRAb) results were positive for 6.06% of patients, indicating the presence of autoimmune thyroid disorders.
Conclusion: High prevalence of thyroid disorders was observed among middle-aged females of northern Pakistan. The clinical, biochemical and symptomatology were extensively studied, and we found substantial variations among patients with hypothyroidism, hyperthyroidism and their sub-clinical forms.
Key words: Thyroid disorder, Pakistan, thyroid profile, TSH, T3, T4.

Introduction

Thyroid disease is a common endocrine disorder in our community, second after Diabetes. The thyroid gland is situated in front of the neck, having two lobes that extend upward over the lower half of the thyroid cartilage and is responsible for controlling the metabolism of carbohydrates, proteins and lipids.[1] It secretes thyroid hormones like T3 and T4, which are under the control of the hypothalamic-pituitary-thyroid (HPT) axis. Iodine is important for the biosynthesis of thyroid hormones. The thyroid gland is the only source of thyroxine, while triiodothyronine is mainly produced from the peripheral conversion of thyroxine to triiodothyronine.[2] The benign thyroid disorders are commonly detected as hyperthyroidism, hypothyroidism, and subclinical states of both conditions.[3]

The Thyroid disorders have a global prevalence of 5-10%,[4] and in the U.S, about 27 million people are diagnosed with those disorders.[4] The prevalence of hyperthyroidism and hypothyroidism in Pakistan is 5.1% and 4.1%, while that of subclinical hyper and hypothyroidism is 5.8%

Corresponding Author:
Sobia Sabir Ali
Department of Diabetes & Endocrinology,
MTI, Lady Reading Hospital, Peshawar.
Email: drsobias@hotmail.com

Received: 20 September 2021, **Accepted:** 12 December 2021,
Published: 16 August 2022

Authors Contribution

FU & SSA conceptualized the project and did the literature search. FU, SSA & HT did the data collection. The statistical analysis, drafting, revision & writing of manuscript were done SSA.

and 5.4%, respectively.[4,5] Its prevalence relies on age, gender, environmental and racial factors, with noticeable numbers in iodine-deficient countries.[1]

Hyperthyroidism or thyrotoxicosis is characterized by the hyperactivity of the thyroid gland, which results in high T3 and T4 levels with suppressed TSH. Its causes are Graves' disease, Toxic Multinodular goitre, acute thyroiditis and solitary toxic adenoma. Among classical complaints are fatigue, anxiety, tachycardia, weight loss and heat intolerance etc. Though it is benign, hyperthyroidism can lead to serious complications like atrial fibrillation (AF), osteoporosis or heart failure.[2] On the other hand, hypothyroidism is characterized by under-activity of the gland with decreased T3 and T4 levels and concomitantly elevated TSH levels. The causes of hypothyroidism can vary from being intrinsic or autoimmune e.g., Hashimoto's thyroiditis to extrinsic causes such as drug induced due to Lithium or Amiodarone.[5] Clinical manifestations could range from mild or no symptoms to severe life-threatening such as that in myxedema coma, which further alters mental health, causes hypothermia, bradycardia, and progressive lethargy, and eventually leads to multiple organ dysfunction syndromes (MODS) and death.[6] In rare instances, severe hypothyroidism can also cause pituitary hyperplasia.[6] Cardiovascular risk increases among patients with hypothyroidism, i.e. hypertension and dyslipidemia are commonly observed.[6] Furthermore, myocardial injuries and pericardial effusions are also common observations among hypothyroid patients as compared to euthyroid.[2] While others are related to neurosensory, musculoskeletal, and gastrointestinal manifestations.

The treatment options for hyperthyroidism or thyrotoxicosis are antithyroid drugs, radioactive iodine and surgery, based on the cause and severity of the disease.[3,4] While levothyroxine, as replacement therapy, is commonly used for hypothyroidism.[1,2] If left untreated, thyroid diseases lead to further complications affecting the patient's quality of life.[2] Subclinical hypothyroidism increases the risk of coronary artery disease (CAD) and atherosclerosis.[3,6] Whereas hyperthyroidism increases the heart rate and enhances the left ventricular mass causing arrhythmias.[6] Many other anomalies related to coagulation, diastolic function, cardiovascular hemodynamics changes, hypercholesterolemia, mental illness, bone demineralization are also associated with thyroid dysfunctions.[7-9]

The interesting observation is that data of thyroid disorders from one population cannot be extrapolated to another. Similarly, in a country like Pakistan with varying geographic landscapes and ethnicities, the in-depth knowledge of prevailing thyroid issues needs to be carefully studied. In support of that, we do not have a rampant coverage of our National Iodine Deficiency Program across the country and more so in the North-Western areas of the country that further necessitates the understanding of different thyroid conditions by the relevant specialists. Therefore, it is essential to conduct a detailed study for determining the clinical profile, etiology and associated co-morbidities of thyroid dysfunction in patients visiting the Endocrinology outpatient clinics. These patients ought to be followed up with an appropriate management plan to look for treatment responses and their primary thyroid disorder complications.

Methodology

A cross-sectional study was conducted at the Department of Diabetes & Endocrinology, Medical Teaching Institution (MTI), Lady Reading Hospital, Peshawar from January to July 2021. A total of 66 subjects aged 16 to 70 years with clinical features suggestive of thyroid disorders were recruited as per the declaration of Helsinki. The patients suffering from diseases such as ischemic heart disease (IHD), chronic kidney disease (CKD), chronic liver disease (CLD), and any acute illness within the past 3 months were excluded. Pregnant and lactating females, patients on drugs like lithium, amiodarone and radioactive iodine were also excluded. The sample size was calculated using the WHO sample size calculator, keeping the 95% confidence level, 5% absolute precision and expected prevalence at 4.1%.[5] The participants were fully informed regarding the study objective and written informed consent was obtained before enrollment.

Patient data, including demographic characteristics, clinical, biochemical and thyroid symptomatology profiles, were collected using a pre-structure, questionnaire. Thyroid Function Tests (TFTs) were performed on Cobas E411 analyzer, with immunoassay analysis done on Electro Chemi Luminescence (ECL) technology to check the levels of triiodothyronine (T3 ng/ml), Thyroxin (T4 ulU/ml) and Thyroid-stimulating hormone (TSH ulU/ml) levels. For quality check, the controls were run by the laboratory staff. (Which ELISA method and what was the quality check). The autoimmune tests for TSH-receptor antibodies (Anti-TRAb) and thyroid peroxidase antibodies (Anti-TPO) were used to diagnose and distinguish the autoimmune thyroid diseases from other forms. Thyroid ultrasound and

radio-nuclear scan were obtained to observe the enlargement, suspicious nodules.

The collected data was analyzed using SPSS version 22.0. The categorical variables were presented as frequencies and percentages. While the continuous variables were given as mean and standard deviation. The clinical, biochemical, and symptom profile variations among hypo and hyperthyroid patients were also studied.

The Ethical approval was obtained from Institutional Review Committee of Medical Teaching Institution, Lady Reading Hospital, Peshawar.

Results

Out of 66 patients included in the final analysis, there were 87.9% females. The mean age of these patients was 40.82±13.77 years. Other socio-demographic characteristics are given in Table-1.

Table 1: Socio-demographic characteristics of the study participants. (n=66)

Variables		*n (%)*
Age (year)		40.82±13.77
Gender	Male	8 (12.1)
	Female	58 (87.9)
Marital Status	Married	60 (90.9)
	Unmarried	6 (9.1)
Educational Status	Illiterate	3 (4.5)
	Literate	63 (95.45)
Occupation	Employed	10 (15.15)
	Unemployed	56 (84.84)

*Values are given as mean±SD or n (%)

Based on the clinical spectrum, hyperthyroidism was diagnosed among 72.7% of the study participants, while 12.1% suffered from hypothyroidism, 9.1% and 6.1% were observed with subclinical hypo and hyperthyroidism, respectively. Furthermore, the mean weight of the patients with hypo and sub-clinical hypothyroidism was more than 60 kg. In contrast, it was significantly low among those with hyperthyroidism and sub-clinical hyperthyroidism, i.e. 45.12±5.89 and 43.0 ±3.46 kg, respectively. Also, Table-2 displays the comparative clinical, biochemical and thyroid symptomatology profile among hypothyroid and hyperthyroid patients.

Diagnostic tests were carried out to determine the etiology of thyroid disease. Anti-thyroid peroxidase (TPO) was within normal limits in most of the participants (95.5%), but 4.54% of Hypothyroid females were found to have elevated thyroid peroxidase antibodies. While TRAb results were positive for 6.06% of Hyperthyroid patients indicating autoimmune disorders.

Discussion

This study explored the different clinical presentations of thyroid disorders at a tertiary care hospital in Peshawar. More than 70% of the enrolled patients had hyperthyroidism, followed by hypothyroidism, subclinical hypo and hyperthyroidism, respectively. In the United States, the reported prevalence of overt hypothyroidism ranges between 0·3 to 3·7%, and it is 0·2 to 5·3% in Europe.[10-12] Furthermore, a similar study from KPK reported that 32.5% of the enrolled population had hyperthyroidism, and hypothyroidism was present among 31.8%, which is comparatively lower than observed in the present study.[5]

Most of the patients with thyroid dysfunctions were females, i.e. 87.9% (Table 1), consistent with the widely recognized global epidemiology of elevated thyroid disease prevalence among females.[11,12] According to a study from Norway, the incidence of thyroid diseases is nearly five-folds higher among females than males.[11] Similarly, other studies from Pakistan, India and Nepal found a higher proportion of female patients, i.e. >70% suffering from thyroid diseases.[7,13,14]

Thyroid disorder has long been recognized as a risk factor for depression and anxiety.[15] A high prevalence of anxiety was found in patients with hyperthyroidism, while depression is commonly reported among hypothyroid patients.[15] In support, we also found that majority of the patients with thyroid dysfunction had neuropsychiatric symptoms, anxiety being the most commonly reported symptom by all the hyperthyroid and sub-clinical hyperthyroid patients. Followed by emotional lability, 54.2% of those with hyperthyroidism suffered from emotional lability, while 12.5% of the hypothyroid patients reported so. In comparison, depression was profound among hypothyroid (87.5%) and sub-clinical hypothyroid (83.3%) patients. Sleep disturbance, poor concentration and memory loss were the other neuropsychiatric symptoms, which were less common. Consistent with this, a number of reported high scores on the anxiety and depression scale among hypothyroid patients and a few report in contrast as well.[15-18] An observational study reported depressive symptoms among 63.5% of the patients with sub-clinical hypothyroidism,[19] while large-scale cross-sectional studies failed to

Table 2: Comparative clinical, biochemical and thyroid symptomatology profile among hypothyroid and hyperthyroid patients.

Variables			*Diagnosis*				*Total*
			A (n=8)	*B (n=48)*	*C (n=6)*	*D(n=4)*	*(n=66)*
Biochemical	Blood Pressure (mmHg)		121.96±24.18	123.01±13.47	114.13±18.57	119.78±7.95	121.88±15.18
	Pulse (bpm)		67.25±8.34	106.37±11.05	164.16±250.75	105.50±4.12	106.83±73.68
	Temperature (ºC)		97.87±0.35	98.08±0.27	98.0±0.00	98.25±0.50	98.06±0.2976
	Weight (kg)		61.25±10.13	45.12±5.89	62.83±9.17	43.0±3.46	48.56±9.61
	Height (ft)		5.03±0.43	5.21±0.43	5.05±0.31	5.12±0.66	5.17±0.43
	BMI (kg/m^2)		25.32±4.17	24.79±3.19	25.51±4.11	16.65±1.18	26.76±32.87
	T4 (ulU/ml)		7.63±13.50	26.83±7.46	8.92±1.65	11.00±1.41	21.92±11.23
	T3 (ng/ml)		86.50±14.57	272.96±97.00	138.50±24.08	151.50±17.00	230.77±112.74
	TSH (ulU/ml)		39.85±0.00	0.02±0.00	21.23±0.00	0.04±0.00	6.78±20.79
Clinical	Palms	Cold	7(87.5)	1(2.1)	5(83.3)	-	13(19.7)
		Sweaty	1(12.5)	47(97.9)	1(16.7)	4(100)	53(80.3)
	Nails	Changes	-	1(2.1)	-	-	1(1.5)
		Normal	8(100.0)	47(97.9)	6(100.0)	4(100)	65(98.5)
	Reflexes	Intact	2(25.0)	39(81.2)	1(16.7)	1(25.0)	43(65.2)
		Absent	6(75.0)	9(18.8)	5(83.3)	3(75.0)	23(34.8)
	Tremor	Present	1(12.5)	46(95.8)	-	4(100.0)	51(77.3)
		Absent	7(87.5)	2(4.2)	6(100.0)	-	15(22.7)
	Thyroid Consistency	Soft	8(100.0)	43(89.6)	6(100.0)	4(100.0)	61(92.4)
		Firm	-	5(10.4)	-	-	61(92.4)
	Lymph Nodes	Palpable	1(12.5)	-	-	-	1(1.5)
		Absent	7(87.5)	48(100)	6(100.0)	4(100.0)	65(98.48)
	Bruit	Present	-	1(2.1)	-	-	1(1.5)
		Absent	8(100.0)	47(97.9)	6(100.0)	4(100.0)	65(98.5)
	Goitre on Ultrasound Neck	Present	1(12.5)	7(14.6)	-	-	8(12.1)
		Normal	7(87.5)	41(85.4)	6(100.0)	4(100.0)	58(87.8)
	Thyroid Texture on Ultrasound	Homogenous	7(87.5)	31(64.6)	6(100.0)	1(25.0)	45(68.2)
		Heterogeneous	1(12.5)	17(35.4)	-	3(75.0)	21(31.8)
	Nodular Morphology of Thyroid on Ultrasound	Single	-	7(14.6)	-	-	7(10.6)
		Multiple	1(12.5)	4(8.3)	-	2(50.0)	7(10.6)
		Absent	7(87.5)	37(77.1)	6(100.0)	2(50.0)	52(78.8)
	Calcification on Ultrasound	Yes	-	2(4.2)	-	-	2(3.0)
		No	8(100.0)	46(95.8)	6(100.0)	4(100.0)	64(97.0)
	Vascularity on Ultrasound	Increased	-	13(27.1)	-	-	97.0%
		Decreased	8(100.0)	35(72.9)	6(100.0)	4(100.0)	53(80.3)
	Radionuclear Scan (Uptake)	Increase	8(100.0)	47(97.9)	6(100.0)	4(100.0)	65(98.5)
		Decrease	-	1(2.1)	-	-	1(1.5)
	Radionuclear Scan (Types of Nodules)	Hot	-	2(4.2)	-	-	2(3.0)
		Cold	-	2(4.2)	-	-	2(3.0)
	Colloid	Yes	-	3(6.3)	-	-	3(4.5)
		No	8(100.0)	45(93.8)	6(100.0)	4(100.0)	63(95.5)
Symptomatology	Constitutional	Weight Loss	1(12.5)	47(97.9)	-	4(100.0)	52(78.8)
		Weight Gain	7(87.5)	1(2.1)	6(100.0)	-	14 (21.2)
		Heat Intolerance	1(12.5)	45(93.8)	-	4(100.0)	50(75.8)
		Cold Intolerance	7(87.5)	1(2.1)	4(66.7)	-	12(18.2)
		Restlessness	1(12.5)	28(58.3)	-	1(25.0)	30(45.5)
		Tiredness	5(62.5)	46(95.8)	4(66.7)	1(25.0)	56(84.8)
		Appetite	4(50.0)	20(41.7)	3(50.0)	-	27(40.9)
		Fatigue	6(75.0)	38(79.2)	5(83.3)	2(50.0)	51(77.3)
		Myalgia's	7(87.5)	36(75.0)	1(16.7)	1(25.0)	45(68.2)
	Cardiovascular	Palpitations	1(12.5)	44(91.7)	-	4(100.0)	49(74.2)
	Respiratory	Dyspnea	3(37.5)	4(8.3)	-	-	7(10.6)

Gastrointestinal	Diarrhea	-	16(33.3)	-	2(50.0)	18(27.3)
	Constipation	7(87.5)	2(4.2)	4(66.7)	-	13(19.7)
Neuromuscular	Difficulty Raising From Chair	7(87.5)	23(47.9)	4(66.7)	1(25.0)	35(53.0)
	Difficulty Combing Hair	6(75.0)	21(43.8)	2(33.3)	-	29(43.9)
	Extremity Shaking	1(12.5)	44(91.7)	-	4(100.0)	49(74.2)
Neuropsychiatric	Sleep Disturbance	4(50.0)	3(6.3)	3(50.0)	-	10(15.2)
	Poor Concentration	3(37.5)	1(2.1)	1(16.7)	-	5(7.6)
	Depression	7(87.5)	12(25.0)	5(83.3)	1(25.0)	25(37.9)
	Memory Loss	1(12.5)	-	1(16.7)	-	2(3.0)
	Emotional Liability	1(12.5)	26(54.2)	-	-	27(40.9)
	Anxiety	1(12.5)	48(100.0)	1(16.7)	4(100.0)	54(81.8)
Genitourinary	Oligomenorrh-oea	-	10(20.8)	-	-	10(15.2)
	Menorrhagia	2(25.0)	1(2.1)	3(50.0)	-	6(9.1)
Skin	Dry Skin	6(75.0)	2(4.2)	4(66.7)	-	12(18.2)
	Discoloration	3(37.5)	1(2.1)	1(16.7)	-	5(7.6)
	Sweating	-	26(54.2)	-	2(50.0)	28(42.4)
	Itchy Skin	6(75.0)	10(20.8)	4(66.7)	1(25.0)	21(31.8)
	Hair Loss	7(87.5)	41(85.4)	6(100.0)	2(50.0)	56(84.8)
Head, Eyes, Ear, Nose & Throat	Thyroid Swelling	8(100.0)	48(100.0)	5(83.3)	4(100.0)	65(98.5)
	Eye Lid Swelling	-	9(18.8)	-	-	9(13.6)
	Double Vision	-	5(10.4)	-	-	5(7.6)

A = Hypothyroidism, B = Hyperthyroidism, C = Sub-clinical Hypothyroidism, D = Sub-clinical Hyperthyroidism
Values are given as mean±SD or n(%)

demonstrate the link between the sub-clinical state of the disease and depression.[17,18] Whereas in another study a high frequency of depression, anxiety, mania, and sleep disturbances was noted amongst hyperthyroid patients.[18,19] Cognitive deficits, poor concentration, compromised planning and productivity were reported as the residual symptoms in patients admitted with hyperthyroidism, observed even after recovery.[19]

Furthermore, variations in the bodyweight were prominent; the mean weight of the patients with hypo and sub-clinical hypothyroidism was high, while it was significantly low among those with hyperthyroidism and sub-clinical hyperthyroidism. Also indicated by the frequency of constitutional symptoms, weight loss and heat intolerance among those with the overactive thyroid gland (97.9% and 93.8%, respectively). Whereas weight gain and cold intolerance were more commonly reported among hypothyroid patients (87.5% for each symptom). Furthermore, loss of appetite was more common among hyperthyroid patients. The existing literature also supports our findings.[20,21] Al Shahrani et al. and Rai et al. also found an association between weight loss and hyperthyroidism, while hypothyroidism was associated with weight gain.[20, 21]

In addition, thyroid swelling was profound among all patients, either presenting with hyper or hypothyroidism, i.e. 98.5% of the total enrolled patients (Table-2). While the gastrointestinal symptoms were not prominent among many cases, i.e. only 27.3% and 19.7% of the total patients had diarrhea and constipation, respectively. A study in Saudi Arabia found that 25.3% of the population recognized thyroid swelling, constipation, and diarrhea as signs of thyroid disease.[22] Moreover, the cutaneous manifestations of these thyroid disorders greatly vary; a study reported skin moistening among 85.7% of patients with hyperthyroidism, while dry, rough skin was observed in 100% of patients with hypothyroidism.[23] Consistent with this, most of the hypothyroid and sub-clinical hypothyroid patients in the present study had dry and itchy skin while sweating was present in >50% of hyperthyroid and 50% of the sub-clinical hyperthyroid patients.

Among the neuromuscular symptoms, shaking of extremities was most frequent, more prevalent among hyper and subclinical hyperthyroid patients than those with hypothyroidism or subclinical state. Followed by difficulty in raising from chair and combing hair, which were more frequent among hypothyroid patients. All of these

manifestations directed muscular dysfunctionality. A study focusing on neuromuscular manifestations reported that muscle dysfunction, including weakness, fatigability, pain and cramps, were frequent among 79% of the enrolled hypothyroid patients while 67% in those with hyperthyroidism.[11,12]

Lastly, oligomenorrhea and menorrhagia were the observed genitourinary symptoms, where oligomenorrhea was only observed among hyperthyroid patients, and 50% of the sub-clinical hypothyroid patients reported menorrhagia. Although, the reported frequency of menstrual problems has decreased lately due to early diagnosis and appropriate management of thyroid dysfunction. Nevertheless, a substantial proportion of women with menstrual problems and fertility issues display endocrine disturbances, specifically hypothyroidism and, to some extent, hyperthyroidism as well.[21] Menstrual problems have been noticed amongst 64.7% of the enrolled hyperthyroid females compared to healthy controls (17.2%).[4,5]

The presence of anti-thyroid peroxidase (TPO), anti-thyroglobulin (Tg), and anti-thyroid-stimulating hormone receptor (TSHR) antibodies are indicative of the autoimmune disorder.[15] High-level anti-TPO titers are observed among 90% of the patients with Hashimoto's thyroiditis, while 10-15% of the normal individuals without any sort of thyroid dysfunction might show these high-level titers but rarely observed.[24] While the highest mean levels of TRAb are observed among the patients with Graves' disease.[24] In the present study, Anti-TPO was present among 4.54% of patients, while 6.06% had positive TRAb results indicating systemic autoimmune diseases. The variation in the initiation of the autoimmune process in the present study compared to that reported in other studies may be due to differences in the genetic, environmental and individual factors that play a key role in the manifestation of autoimmune thyroiditis.[25]

In conclusion, hyperthyroidism was the most prevalent among the enrolled patients. There is a prominent variation in the clinical spectrum of thyroid diseases that should be considered for appropriate diagnosis. Furthermore, weight gain, weight loss, cold, heat intolerance, anxiety, depression, hair loss and tremors are some of the clinical and symptomatic features that help distinguish the under and overactive thyroid cases.

The interesting point is that data on thyroid disorders from one population cannot be extrapolated to another. Similarly, in a country like Pakistan, with its diverse geographic environments and ethnicities, a thorough understanding of thyroid-associated manifestations and clinical features is required. Practical health education approaches by health authorities are highly recommended for further exploration of the disease. Our study is limited by the small sample size, with no control group and the cross-sectional design. Large-scale, extended follow-up studies with diverse populations are required to assess the comparative and long-term complications of the disease among people of different parts of the country.

Conflict of interest: None declared.

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