PREVALENCE AND MANIFESTATIONS OF THYROIDAL DYSFUNCTION IN CENTRAL PUNJAB PAKISTAN (A CASE STUDY)

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ABSTRACT: Thyroid gland is a major endocrine player in maintaining homeostasis of the body by the production of vital endocrine hormones, thyroxine (T4) and tri-iodothyroinine (T3). The prevalence of thyroidal ailments is rapidly increasing worldwide mostly in developing countries like Pakistan. Not being life threatening, these disorders are mostly overlooked and delayed until they transform into a cancerous form and become a risk for life. Besides this, the malfunctioned gland greatly affects the functioning of other organs of the body that rely on its secretion for normal functioning. To figure out the situation of thyroidal disorders in Central Punjab, present study was found to be mandatory. For this purpose INMOL Hospital Lahore was visited from January 2014 to December 2015 to find out the prevalence of this ailment in our local population. Newly diagnosed patients were enrolled in the study and their signs and symptoms were recorded. Thyroid function test (TFT) was performed by Radio Immuno Assay (RIA). The prevalence of different signs and symptoms related to thyroid dysfunction was also analyzed and relation of these symptoms with the disease was determined. Our study showed increased prevalence of hyperthyroidism with more number of female patients. The incidence of goiter in hyperthyroid state was 44%, whereas in hypothyroid patients, it was observed at 27%. Prevalence of both hyper and hypothyroidism was high at 21-30 years of age, whereas, hyperthyroidism was also found to be prevalent at 41-50 years of age.
Keywords: Hyperthyroidism, Hypothyroidism, T3, T4, TSH

INTRODUCTION

Perturbation in hypothalamus-pituitary-thyroid axis (HPT) usually affects the whole body mechanisms by disturbing thyroid function [1]. Thyroidal ailments and diabetes mellitus are most common glandular disorders all around the world, irrespective of the gender and age [2], [3]. Most thyroid hormone derangements may vary from subclinical which is asymptomatic with abnormal TSH level and normal free T3 and T4 levels to clinically symptomatic with abnormal T3 and T4 levels [4]. Besides this, common thyroid dysfunctions include subclinical phases, goiter, iodine deficiency disorders, Hashimoto's thyroiditis, Graves disease and thyroid cancer [5]. These disorders have been reported in over 110 countries of the world with 1.6 billion people at risk [6].

Iodine is essential for producing T3 and T4 [7]. Availability of iodine to thyroid gland is mainly from food and water and if these sources are deficient in iodine, problems like hypothyroidism, cretinism and other iodine deficiency disorders can progress [8]. Iodine deficiency usually prevails over one third part of the world [9]. The prevalence of goiter in areas of severe iodine deficiency can be up to 80% [10]. Iodine deficiency is the basis of high prevalence of thyroid disorders in South Asian population as well [9]. In many cases mainly goiter is the sole reason for patient to screen for thyroid disorder by their physician. Prevalence as high as 12% and 23% of goiter has been reported in India in adults [11] and children [12], respectively. In Pakistan, the prevalence of overt and sub clinical hyperthyroidism is reported to be 5.1% and 5.8%, respectively. Similarly, the prevalence of overt and sub clinical hypothyroidism is observed at 4.1 and 5.4%, respectively. It is also perceived that the prevalence of both hyperthyroidism and hypothyroidism (subclinical or overt) is higher in females than males [13].

Abnormalities in subclinical hypothyroidism are associated with increased risk for atherosclerosis and coronary artery disease [14]. Ailments found in subclinical hyperthyroidism are increased heart rate, prevalence of supraventricular arrhythmias and enhanced left ventricular mass [15]. In the same way overt thyroid dysfunction, whether overt hypothyroidism or overt hyperthyroidism, show coagulation abnormalities [16], various alterations in cardiovascular hemodynamics, endothelial dysfunction, diastolic function abnormality [14], hyperhomocysteinemia and hypercholesterolemia [17].

In iodine-sufficient areas, autoimmune thyroid disease and thyroablative therapy are the major reasons of hypothyroidism even in children and adolescents [18]. The untreated thyroidal disorders can manifest serious consequences especially cardiovascular diseases [19]. Hence, improved public awareness about thyroidal ailments is one of the important factor to cope with this disorder. This cross sectional study aims at determining the clinical features and pathophysiological aspects of thyroidal ailments present in our population.

MATERIALS AND METHODS

This cross sectional study centered around 472 newly diagnosed patients of hypo- and hyperthyroidism registered at Institute of Nuclear Medicine and Oncology, Lahore from January 2014 to December 2015. Subjects were interviewed for their signs and symptoms as well as their clinical and family history of thyroid disorders. Subsequently, their blood samples were drawn and preserved at -80°C. They were clinically categorized into hypo- and hyperthyroidism, as well as in their subclinical states by the thyroid function test utilizing RIA. Patients having clinically visible enlarged swelling in front of neck were subjected to ^{99}Tc Pertechnetate thyroid imaging.

Statistical analysis was performed using graph pad prism 7 series. Our study included subjects of all ages and both genders. Patients having complications of obesity, diabetes mellitus, hypertension, hepatitis, cardiovascular disorders and pregnancy were excluded from our study. An informed

consent was obtained from each individual participant and all the subjects were interviewed for collecting demographic and disease data on pre designed questionnaire. Initial screening included complete thyroid profile to identify and categorize patients into subclinical and overt hypo- and hyperthyroid states.

RESULTS

A total of 472 patients having either form of thyroidal dysfunction were included in the study. Body Mass Index (BMI) of these patients was calculated after measuring their body weight in kg and height in m^2 and their mean and standard deviation was calculated. The BMI was found to be the lowest in overt hyperthyroid group i.e., 20.66±3.78 kg/m^2 due to weight loss, and was highest in overt hypothyroid group i.e., 25.68±3.84 kg/m^2 due to general trend of weight gain in this group. BMI of sub clinical hyperthyroid and hypothyroid groups was 24.42±5.53 kg/m^2 and 23.96±2.75 kg/m^2, respectively. Although the values of BMI were not much varied yet they showed a general trend of increased weight in hypothyroid state and weight loss in hyperthyroid patients having normal values with a slight difference in subclinical states (Table 1).

Table 1
Biochemical and Physical Parameters in the Subjects of study

	Overt Hyperthyroid (Mean ± S.D)	Subclinical Hyperthyroid (Mean ±S.D)	Overt Hypothyroid (Mean± S.D)	Subclinical Hypothyroid (Mean ±S.D)
BMI (kg/m2)	20.66±3.78	24.42±5.53	25.68±3.84	23.96±2.75
FreeT3 (pmol/l)	26.93±11.06	4.47±0.53	2.31±1.08	3.68±0.92
FreeT4 (pmol/l)	47.85±13.72	17.91±3.85	7.41±4.70	14.98±3.12
TSH (mIU/l)	0.03±0.03	0.12±0.09	36.22±14.24	8.05±0.59

The subjects underwent thyroid function test (TFT) for the measurement of fT3, fT4 and TSH and compared with normal ranges of fT4 (11.5-23.0 pmol/l), fT3 (2.5-5.8 pmol/l) and TSH (0.3-5.0 mIU/l). The mean value of fT3 and its standard deviation was calculated and it was found that its value was higher i.e., 26.93±11.06 pmol/l in overt hyperthyroidism. Whereas, there was decreased concentration of this hormone in overt hypothyroid state i.e., 2.31±1.08 pmol/l and normal values in subclinical hyperthyroid and hypothyroid state i.e., 4.47±0.53 pmol/l and 3.68±0.92 pmol/l, respectively. Similarly, the mean value of fT4 was quite higher i.e., 47.85±13.72 pmol/l in overt hyperthyroid and lower in overt hypothyroid patients group i.e., 7.41±4.70 pmol/l. Normal ranges were observed in subclinical hyper and hypothyroid states i.e., 17.91±3.85 pmol/l and 14.98±3.12, respectively. Mean values of TSH were found to be decreased in overt hyperthyroidism, whereas, greatly increased in overt hypothyroidism. It was also abnormally elevated in subclinical hypothyroid patients which was 8.05±0.59 mIU/l, whereas, normal value was observed in subclinical hyperthyroid patients i.e., 0.12±0.09 mIU/l (Table 1).

Our investigation revealed that out of 472 patients, 144 (30.5%) were having age below 25 years. However, 328 (69.5%) subjects selected in our study were above 25 years of age. It was observed that the people above 25 years of age were more vulnerable to thyroidal disorders (Table 2).

Table 2
Age Distribution of Hypo- and Hyperthyroidism in Population

	Age ≤ 25		Age 26 ≥ 100	
Diagnosis	**Male**	**Female**	**Male**	**Female**
Hypothyroidism	8	28	24	88
Hyperthyroidism	24	84	48	168

Regarding gender distribution, out of 472 subjects, 200 (42.4%) females and 56 (11.9%) males were affected with overt hyperthyroidism. Whereas, the incidence of subclinical hyperthyroidism in females and males was 52 (11%) and 16 (3.39%), respectively.

Table 3 Gender Distribution amongst different clinical state

Gender	Overt Hyper	Subclinical Hyper	Overt Hypo	Subclinical Hypo
Male	56	16	12	8
Female	200	52	96	32

In case of hypothyroidism, overt clinical state was more commonly found in females affecting 96 (20.3%) females and 12 (2.54%) males. Whereas, subclinical hypothyroidism affected 32 (6.8%) females and 8 (1.69%) males. Overall in subjects studied, 68.64% were suffering from hyperthyroid state and 31.36% subjects were suffering from hypothyroidism (Table 3).

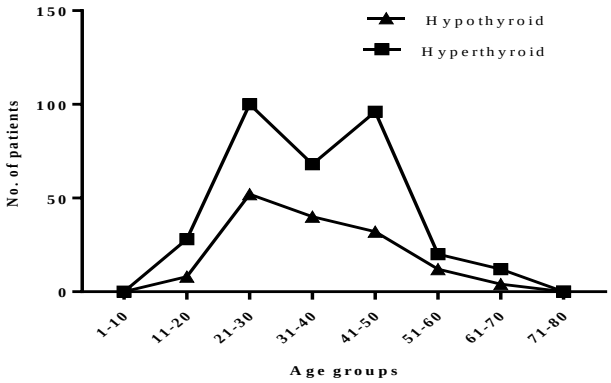

Fig. 1. Age distribution in Hyper and Hypothyroidism.

In our findings thyroidal dysfunction illustrated a bimodal age distribution in hyperthyroidism showing first peak around 21-30 and second peak around 41-50 years of age. However, in case of hypothyroid state, only a single peak was observed between 21-30 years of age (fig.1).

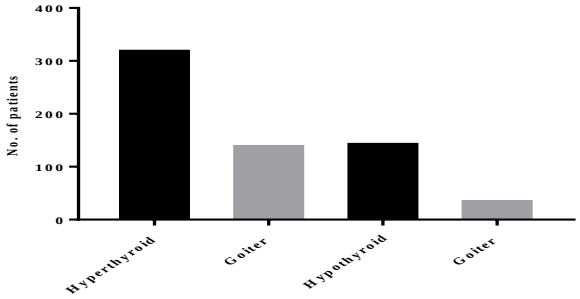

Fig. 2. Number of patients presenting goiter.

In case of hyperthyroid clinical phase, 144 of the subjects i.e., (44.4%) were found to have goiter. Whereas, 40 of hypothyroid subjects i.e., (27%) were suffering from goiter (fig.2).

Table 4 Categorical variables of Patients

Demographic Features and signs	Hyperthyroid (n=324)		Hypothyroid (n=148)	
	%ages	Cases	% ages	Cases
Location		N		N
Urban	70.1	227	72.9	108
Rural	30	97	27	40
Life Style				
Sedentary	75.9	246	62.2	92
Active	24.1	78	37.8	56
Salt Intake				
Non-Iodinated	25	81	43.2	64
Iodinated	75	243	56.8	84
Feeding habit				
Veg	67.9	220	83.1	123
Non-Veg	32.1	104	16.9	25
Weight				
Loss	84.9	275	-	-
Gain	-	-	68.2	101
Goiter				
Female	39.5	128	24.32	36
Male	4.9	16	2.7	4
Bleeding Gum	32.1	104	35.1	52
Muscle aches	48.1	156	67.6	100
Loose stools	25	81	-	-
Skin problem	32.1	104	23	34
Depression	75.9	246	81.1	120
Anxiety/Panic attacks	71	230	64.2	95
Exhausted after sleep	50	162	80.4	119
Constipation	-	-	64.2	95
Throat discomfort	61.1	198	58.8	87
Hair loss	64.2	208	66.9	99
Menstrual irregularities	45.1	146	46.6	69
Heat intolerance	79.9	259	-	-
Periorbital edema	-	-	57.4	85
Peritibial edema	-	-	61.5	91
Hoarseness	-	-	62.2	92
Palpitation	61.7	200	-	-
Sweating	44.4	144	-	-
Exophthalmos	22.2	72	-	-
Tremors	44.4	144	-	-
Shortness of Breath	58	188	-	-
Cold intolerance	-	-	53.4	79
Reduced Sleep	37	120	-	-
Obstructive Sleep apnea	-	-	32.4	48
Appetite	24.7↑	80	21.6↓	32
Fatigue	38.3	124	-	-
Lethargy	-	-	45.9	68

Common symptoms observed in hyperthyroid patients were weight loss, palpitations, and shortness of breath, heat intolerance, tremors, sweating, muscle pain, depression, anxiety, joint pain, gum diseases, fever restlessness and increased appetite. Hypothyroid patients commonly experienced weight gain, muscle pain, depression, feeling exhausted after sleep, constipation, neck discomfort/pain, hair loss, menstrual irregularities in females, periorbital and peritibial edema, hoarseness, eye pain, dry hair, cold intolerance, sleep disturbances. Table 4 is showing the number of cases and the percentages of different demographic features and signs and symptoms of the disease with increase prevalence of thyroid disorders in the people dwelling in urban areas, people with sedentary life style, and vegetarians.

DISCUSSION

Thyroid hormone are necessary for normal growth, development, metabolic regulation neuronal differentiation, in mammals [20,21,22] and are required for metamorphosis in amphibians [23]. These actions are most apparent in conditions of thyroid hormone deficiency leading to hypothyroidism [9], or hyperthyroidism a condition arise due to excess of thyroid hormone production [24]. Thyroidal events are usually the result of different contributing factors like geographical distribution, food habits, dietary iodine consumption and genetic predisposition [25].

The present study was aimed to determine the pathophysiological manifestations of thyroidal dysfunction in central Punjab. In our study, among 324 hyperthyroid patients, 74% were females and 26% were males, while in hypothyroid group having 148 subjects, there were 84% females and 16% males which showed that females are more prone to have thyroid disorders. Hyperthyroidism is reported to be more common in women (2% to 5%) with female to male ratio up to 5:1 between the ages of 20-40 [4]. However, in this investigation female to male ratio is 3.5:1. Over all the ratio of hyperthyroidism to hypothyroidism is 2:1, there is increased prevalence of overt hyperthyroid state especially in females. Age distribution graph, in our study, presents a bimodal distribution showing first peak around 21-30 and second peak around 41-50 in case of hyperthyroidism. Many studies have also reported the increase in the prevalence of thyroid disorders in middle age [10, 26].

Prevalence of overt hyperthyroidism is about 0.5%. However, 1% to 2% of patients have a below-normal TSH level. Low TSH is seen in 3% of the population older than 80 years [27]. High prevalence of hyperthyroidism in Pakistani population is reported by several studies. Being an iodine deficient region the increased prevalence of hyperthyroidism might be due to autoimmune disorder or due to inconsiderate use of iodized salt in the diet due to which thyroid gland becomes hyper functional leading to the state of hyperthyroidism. However, in Western countries there is an increased prevalence of hypothyroid state. In women, high degree of hypothyroidism points to the role of gestational factors that might have contributed to the autoimmunity against the thyroid gland resulting in its destruction [28, 29].

Most thyroid dysfunctions are autoimmune in nature; Graves's diseases accounts for the thyrotoxicosis and Hashimoto's thyroiditis for hypothyroidism [30]. Goiter is one of the leading outcome of the altered thyroid biology. In our data 44.4% of the hyperthyroid patients presented goiter and among hypothyroid patients, 27% were having goiter with more number of female subjects in both groups. The occurrence of goiter and thyroid disease is determined by complex interplay among gender, environmental and genetic factors, and the major environmental factor that determines the goiter dominance is iodine intake status [31]. In addition to this, higher prevalence of goiter among female is attributed to proliferative effect of esterogen on thyrocytes in the thyroid gland [32].

The individuals in hypothyroidism feels weakness, constipation dry and coarse skin cold intolerance reduced and slow metabolic activity and depression [8]. In our investigation, common symptoms observed in hypothyroid state were cold intolerance (53.49%), constipation (64.2%), depression (81.1%), weight gain (68.2%), muscle aches (67.6%), menstrual irregularities (46.6%), hoarseness (62.2%) and obstructive sleep apnea (32.4%).

Clinically profound symptoms of the hyperthyroidism are weight loss, increased hunger, weakness, and tremors of hands, elevated heartbeat, goiter, loose stools, anxiety, exophthalmos, increased sweating, and heat intolerance [33], [34]. In this study, clinical symptoms of hyperthyroidism are frequent bowl movements (25%), skin problem (32.1%), menstrual irregularities (45.1%), weight loss (84.9%), palpitations (61.7%), and shortness of breath (58%), heat intolerance (79.9%), tremors (44.4%), sweating (44.4%), muscle aches (48.1%), anxiety (71.1%) and increased appetite (24.7%).

Hypothyroidism is profoundly associated with deranged lipid levels resulting in the manifestation of atherosclerosis. Utilization of the lipoid substances are promoted by the thyroid hormones and their substrates, triggering an increased mobility of the triglycerides which are stored in the adipose tissue. Overt hypothyroidism, with its accompanying hypercholesterolemia and hypertension, has been found to be associated with cardiovascular disease [36]. In our study an approximately 7% of the females and 2% of the male patients were suffering from subclinical hypothyroidism, however in the Rotterdam survey 11% of the females were reported to have subclinical hypothyroidism. Hak *et al.,* (2000) have reported an increased prevalence of subclinical hypothyroidism among women accompanying with a greater aortic atherosclerosis and myocardial infarction. These events were marginally evident in those women, having antibodies against thyroid peroxidase [37].

CONCLUSION

Public awareness about the dietary iodine consumption is mandatory in our region, so as to overcome the increased prevalence of the thyroidal dysfunction in our population. Furthermore, hyperthyroid state is more obvious in our population as compared to hypothyroidism in both genders.

ACKNOWLEDGEMENTS

Authors of the present study greatly acknowledge Dr. Abubakar Shahid, Director Institute of Nuclear Medicine and Oncology, Lahore for his key advices in the data collection procedure. Higher Education Commission of Pakistan is highly appreciated and obliged for providing financial assistance for the study.

DECLARATION OF INTERESTS

It is hereby declared that the research article entitled as "Clinical prevalence and manifestation of thyroidal dysfunction in Central Punjab", submitted by M. Amir Iqbal, Zahra Naseem, Dr. Ahmad Qureshy, Dr Abubakar Shahid and Dr. Nabila Roohi for publication in your research journal is (i) neither submitted anywhere nor any part of the work is submitted elsewhere, (ii) there is not a single conflicts related to this manuscript, (iii) the study is financed by Higher Education Commission of Pakistan vide letter No.112-33289-2BMI-342(50022893) and (iv) the manuscript has been read by all authors, fulfills the requirements for authorship, and represents the original work of the authors.

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