Original Article

Epidemiologic Profile of Thyroid Disorders in a Tertiary Care Hospital, a Five Years Analysis

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Abstract

Background: Thyroid disorders are commonly encountered endocrine ailments in clinical practice.

Objective: To determine the trends and frequency of thyroid disorders in patients presented for thyroid dysfunction at the department of Pathology Benazir Bhutto hospital Rawalpindi

Study Design: Cross-sectional retrospective study.

Materials and Methods: Patients who underwent thyroid function tests were enrolled in the study Thyroid function tests were performed on a fully automated Chemistry Analyzer. Graph Pad Prism version 7 and SPSS version 25 were used for statistical analysis of the data.

Results: Out of 2856 patients, 81.9% were females and 18.1% were males. The mean age of the participants was 38.12 ± 14.51 years and the median was 35(13-96). Overall, 1951 (68.3%) of the subjects were euthyroid, 343(12.0%) had subclinical hyperthyroidism, 200 (7.0%) had subclinical hypothyroidism, 192(6.7%) had overt hyperthyroidism and 168 (5.9%) had overt hypothyroidism. Females have a significantly high percentage of thyroid disorders as compared to males($\chi 2$ =0.976 p =0.027). The major age group 798(27.9 %) tested for thyroid dysfunction suspicion was 24 to 33 years followed by 34-43 (22.9%).

Conclusions: The thyroid dysfunction prevalence was higher in females than males. An upward trend in the frequency of thyroid dysfunction was observed with increasing age. Subclinical hyperthyroidism was the commonest abnormality observed. A steep rise in subclinical hyperthyroidism may be attributed to the high intake of iodized salt.

Keywords: Epidemiology, Thyroid dysfunction, TSH, T3, T4, iodized salt, Pakistan.

Introduction

Impaired thyroid function:

In clinical practice, thyroid ailments are frequently encountered endocrine disorders next to diabetes.[1,2] They arise either due to functional aberrations of the thyroid gland resulting in over or under secretion of thyroid hormone or due to the development of structural anomalies. Thyroid hormones are synthesized by the endocrine gland present in the neck. Thyrotropin also known as Thyroid-stimulating hormone (TSH), is released from the pituitary gland, regulates the synthesis of thyroid hormones.[3] It stimulates the thyroid gland to synthesize thyroxine (T4) and 3,5,3'-triiodothyronine (T3) which after being released in circulation work in synchrony with the upstream modulators and keep a proper feedback mechanism to maintain the body's homeostasis. Due to the highly variable and mostly non-specific clinical presentation of thyroid disease, the diagnosis of thyroid dysfunction is mainly based on biochemical validation. The intricate inverse relationship between TSH, T4, and T3 renders serum TSH analysis the first line marker for screening of thyroid disorders. Serum T3 and serum T4 are measured if TSH concentrations do not fall within the normal reference range.[4,5] Accordingly, frank hyperthyroidism is defined as TSH level below the reference range and T4 concentration above the reference range while subclinical hyperthyroidism is defined as TSH levels below the reference range, but T4 levels within the reference range6. Similarly, the opposite hormone pattern is used to define overt (high TSH, low T4, T3) and subclinical hypothyroidism (high TSH, normal T4).

The thyroid gland exhibits a distinct association with the environment. It is sensitive to iodine intake and thyroid function disruptors. It requires an optimal amount of Iodine (150-250 ug /day) to function appropriately.[1] A major proportion of the global population is residing in iodine-deficient areas. Disproportionate iodine intake in the diet may lead to hypo or hyperthyroidism[7,8] followed by a sequel of disorders i.e. obesity[9], diabetes[10], hypertension[11], cardiovascular complications[12], subfertility, and infertility.[13] The reported incidence of thyroid dysfunction varies geographically, in part due to dissimilarities in disease definitions, iodine intake, inconsistent methods for measuring thyroid function, and diversity in populations.

People have varied constitutional, non-specific manifestations that turn out as abnormal metabolic functioning of the thyroid gland. Over time improved excess to diagnostic modalities, has led to the earlier recognition of thyroid disorders reflected as a considerable increase in Thyroid function tests (TFTs) performed in the Special chemistry Lab. The prevalence of thyroid dysfunction is on the rise worldwide mostly in developing countries like Pakistan.[14] Keeping in view the gravity of the problem current study was undertaken to assess the occurrence of thyroid disorder in subjects visiting the outdoor patients' ward for thyroid function tests.

Materials and Methods

A total of 5258 subjects suspected of thyroid dysfunction were presented to the outpatient department of Pathology Benazir Bhutto hospital. Patients with missing data or incomplete thyroid profile tests and those who had a repeated test or previously diagnosed thyroid disease were excluded. Screening for thyroid dysfunction was based on the thyroid-stimulating hormone, T3 and T4 concentrations. The thyroid profile was assessed by chemiluminescence assay on Vitros special Chemistry Analyser. Subjects were categorized into six age groups to estimate the prevalence of different thyroid disorders in different age groups. The age group division was group 1(13-23 years), group 2 (24 – 33 years), group 3(34-43 years), group 4(44-53 years), group 5(54-63 years), and group 6(64 and above).

SPSS version 25 and Graph pad prism 7 were used to analyze the data. A Chi-Square test was applied to estimate the status of thyroid dysfunction in the study population. The prevalence of thyroid disorders was presented as frequencies and percentages. Due to the highly skewed distribution of thyroid profile tests (T3, T4, and TSH) Kruskal Wallis test was used to compare median levels between both genders and among different age groups. Independent sample t-test and ANOVA were used to compare means of age in both genders and different age groups, respectively. P-value equal to 0.05 was taken as statistically significant.

Operational definitions of Thyroid disorders

Conditions	TSH	T3	T4
Euthyroide	0.3-5 mIU/L	69-202ng/ml	4.5-11.3ug/dl
SC-Hypothyroidism	> 5 to< 9.9 mIU/L	Within reference range	Within reference range
Hypothyroidism	> 10 mIU/L	low	low

SC-Hyperthyroidism	>0.2to<0.3	Within reference range	Within reference range
Hyperthyroidsm	<0.2	high	high
Secondary Hyperthyroidism	Low	low	low

Results

Out of 5258 patients, the highest number (29.3%) was presented for thyroid function tests in 2019. A total of 2856 patients, 2339 (81.9%) females, and 517 (18.1%) males were included in the final analysis. The mean age of the participants was 38.12 ± 14.51 years and the median was 35(13-96). Females presented for thyroid function test at a significantly younger age (37.45± 13.70vs 41.14 ±17.13 p value= 0.001) than males. Concentrations of T3, T4, and TSH were significantly high in females compared to males (Table 1)**.** Overall 68.3% of the subjects were euthyroid, 12.0% had Subclinical-Hyperthyroidism, 6.7% had overt hyperthyroidism, 7.0% had subclinical-hypothyroidism and 5.9% were suffering from overt hypothyroidism (Table 2). Only two cases of secondary hyperthyroidism were identified. The highest percentage (40.6%) of thyroid dysfunction was found in the 54-63years age group and the lowest (19.8%) in 13-23 years. Among male patients 23(4.4%) were hyperthyroid, 28 (5.4%) were hypothyroid 36 patients (7.0%) were suffering from subclinical hypothyroidism and 49(9.6%) had hyperthyroidism. Additionally, in the female population, hyperthyroidism was found in 169(7.2%), 164 (7.0%) had hypothyroidism, 294(12.6%) had subclinical hyperthyroidism and 140(6.0%) had subclinical hypothyroidism. The Incidence of thyroid dysfunction was significantly high in females as compared to males χ^2=12.62 p =0.027

Subclinical Hyperthyroidism

In the current study, subclinical hyperthyroidism (SC-HYPER) was the principal thyroid disorder affecting 12.00 % of subjects, with higher incidence rates (12.6%) in females compared to (9.5%) males. Additionally, the highest prevalence rate of SC-HYPER was observed in 53-64 years, followed by ≥ 64 years and lowest in the 13-23 years age group. An upward trend in incidence rates of SC-HYPER was observed with increasing age.

Subclinical Hypothyroidism

The second most prevalent thyroid disorder in the current study was SC-hypothyroidism (SC-HYPO). Overall, 200(7.0%) of the cases, both males 36(7.0%) and females 164(7.0%) were observed to be equally affected by this disorder. Among females, the highest frequency (19.4%) of SC-hypothyroidism was observed in group 5 (54-63 years) followed by group 6(≥64 years)

Overt Hyperthyroidism

Frank Hyperthyroidism was found to be the third highly prevalent thyroid (6.7%) disorder. More females were 169(7.2%) diagnosed with overt hyperthyroidism compared to 23(4.4%) males. In females, the highly affected age group was [54-63; 28(13.3%)] while in males it was [34-43 45(8.1%)]. Additionally, in females second highly affected age group was [44-53; 50(11.4%)

Overt Hypothyroidism

Overt hypothyroidism is observed to be the least prevalent thyroid disorder with high prevalence rates in females. Overall, 168(5.9%) subjects including 140(6.0%) females and 28(5.4%) males were diagnosed with overt hypothyroidism. Both in males 11(11.6%) and females 45(8.1%) highly affected age group was 34-43. The highest percentage of the patients affected by hyperthyroidism (18.2%) and SC-HYPER (11.5%) fall in the age bracket (54-63). Contrarily, more number of subjects affected by hypothyroidism (8.6%) and SC-HYPO (9.3%) belonged to age groups (34-43) and (44-53) respectively.

Table 1: Baseline characteristics of the subjects at presentation

Parameters	***Over All***	***Females***	***Males***	***p-value***
Age (years)	38.12± 14.51	37.45± 13.79	41.14± 17.13	0.001
T3 ng/dl	117 (1.46-552)	118(6.02-552)	110 (1.46-454)	0.001
T4µg/ml	8.46 (0.45-120)	8.56 (0.45-120)	7.97 (0.74-23)	0.001
TSHµIU/ml	1.40 (0.004-100)	1.38 (0.004-100)	1.50 (0.004-100)	0.031

Table 2: Thyroid function status of Male and Female in different Age groups

Age	*EUTHY*	*SC- HYP*	*SC-HYPER*	*HYPER*	*HYPO*	*P-value*
13-23	274(79.7%)	18(5.2%)	28(8.1%)	8(2.3%)	16(4.7%)	
24-33	481(70.6%)	49(7.2%)	78(11.5%)	40(5.9%)	32(4.7%)	
34-43	373(66.7%)	35(6.3%)	71(12.7%)	34(6.1%)	45(8.1%)	0.001
44-53	257(58.8%)	44(10.1%)	57(13.0%)	50(11.4%)	29(6.6%)	
54-63	118(55.9%)	9(4.3%)	41(19.4%)	28(13.3%)	15(7.1%)	
≥64	67(62.6%)	9(8.4%)	19(17.8%)	9(8.4%)	3(2.8%)	
Female	**1570(67.1%)**	**164(7.0%)**	**294(12.6%)**	**169(7.2%)**	**140(6.0%)**	
13-23	67(82.7%)	7(8.6%)	1(1.2%)	2(2.5%)	4(4.9%)	0.005
24-33	95(81.2%)	8(6.8%)	5(4.3%)	6(5.1%)	3(2.6%)	
34-43	62(65.3%)	7(7.4%)	8(8.4%)	7(7.4%)	11(11.6%)	
44-53	64(70.3%)	5(5.5%)	16(17.6%)	1(1.1%)	(5.5%)	
54-63	52(69.3%)	5(6.7%)	11(14.7%)	5(6.7%)	2(2.7%)	
≥64	41(70.7%)	4(6.9%)	8(13.8%)	2(3.4%	3(5.2%)	
Male	**381(73.7%**	**36(7.0%)**	**49(9.5%)**	**23(4.4%)**	**28(5.4%)**	
All	1951(68.3%)	200(7.0%)	343(12.0%)	192(6.7%)	168(5.9%)	0.001

Discussion

Any changes in the thyroid function status have important clinical implications on human well-being. The prevalence of thyroid disorders varies across the world depending on geographical location, ethnicity, sex, and iodine intake.

The prevalence of thyroid disorders was assessed in adults presented for a thyroid function test. Thyroid dysfunction was observed in 31.7% of the adults with higher prevalence rates (26.8%) in females compared to (4.9%) males. Our results collude with two tertiary care hospital-based studies from India, where thyroid dysfunction affected 31% of adults and was more prevalent in females (27%) than in males (4%).[15] In another hospital-based study prevalence rate of thyroid dysfunction was 22.16%.[16] In Spain, 10% of the population had some form of thyroid dysfunction.[17] Current findings of female predisposition to thyroid dysfunction collude with many other local and international studies.[15,16,18,19] This female preponderance is hypothesized to be due to the effects of female gonadal hormones (most likely estrogens) and X chromosome inactivation in thyroid tissue.[20]

In the current study, 7.0% of the subjects (both genders) were found to be affected by SC hypothyroidism whereas 6% of females and 5.4% of males were affected by overt hypothyroidism. The prevalence rate of SC hypothyroidism in a cohort from Karachi Pakistan has been reported as 9.2% in males and 13.6% in females.[21] In another study from the same city, the frequency of this disorder was reported as 9.4%.[22] In America, 4.0% of women aged 18-24year were affected by hypothyroidism compared to 21% of women ≥ 74 years of age; corresponding percentages in men were 3% and 16%.[23]

Worldwide studies conducted in the previous two decades stated the prevalence of subclinical hypothyroidism in the adult population between 4–20% and the prevalence of sub-clinical hyperthyroidism between 0.7–9%.[23-26] In the current study subclinical hyperthyroidism was observed to be the most prevalent thyroid disorder affecting 12.6% females and 9.5% of males. Followed by subclinical hypothyroidism affecting 7% of the whole study population. Previously a study from Khyber Pakhtoon Khaw described prevalence rates of hyperthyroidism and subclinical hyperthyroidism as 5.1% and 5.8% respectively. In the same study frequency of hypothyroidism and subclinical hypothyroidism was shown to be 4.1% and 5.4% respectively.[27] Recently, a study conducted at Gujranwala institute of nuclear medicine stated that 37% of females and 43% of males were hyperthyroid whereas 16% of females and 23% were hypothyroid. The higher prevalence of hyperthyroidism in this study was attributed to the indiscriminate use of iodized salt.[18]

In the mid-1960s, the Pakistani Government encouraged the use of iodized salt to limit the occurrence of thyroid dysfunction as a preventive health care measure. Salt iodization is a cost-effective way of optimizing iodine intake in the affected population. The incidence of hyperthyroidism after the adoption of iodized salt has been reported by several local and international studies.[7,8,28-30] In Tasmania, the use of iodine fortified bread salt led to a higher incidence of overt hyperthyroidism.[31] Likewise, in

Switzerland and Austria, an increase in iodine content of salt triggered a substantial rise in cases of thyrotoxicosis.[32] High prevalence rates of subclinical and overt hyperthyroidism in the current study may be linked to inappropriate use of iodine fortified salt or due to autoimmune disorder.

Additionally, growing exposure to thyroid-disruptors (TDs) could be another cause of a higher incidence of thyroid dysfunction. According to the novel approach, TDs include bioactive compounds from the food chain and synthetic chemicals that affect any aspect of thyroid hormone (TH) metabolism from synthesis and secretion to transmembrane transport and local actions of thyroid hormone. Pesticides from vegetable cultivation, polybrominated diphenyl ethers bisphenol A and phthalates from containers for food storage and cooking are a few relevant TDs that affect people through diet.[33]

Cardiovascular physiology is affected by subtle changes in TH due to the presence of TH receptors in the vascular tissue and myocardium. The probable mechanisms that associate CV disease with thyroid dysfunction are fluctuations in blood pressure, dyslipidemia, endothelial dysfunction, and myocardial systolic and diastolic dysfunction. Untreated hyperthyroidism is associated with heart failure and atrial fibrillation by increasing cardiac output and left ventricular hypertrophy in the initial stage and dilated cardiomyopathy in the late stage. Similarly, hypothyroidism and SC-HYPO are linked with coronary artery disease, dyslipidemia, and reduced cardiovascular contractility.[34] Overt thyroid dysfunction leads to menstrual irregularities, fertility complications, and pregnancy problems and is often linked with adverse outcomes.[35]

Conclusion

An upward trend in the prevalence of thyroid dysfunction was observed with increasing age. Sub-clinical thyroid disease adds an entirely new dimension to the field of thyroid hormonal imbalance. It needs a cautious approach regarding management. Continuous monitoring of iodine supplementation should be done in the people at risk of developing hyperthyroidism to limit the indiscriminate use of iodized salt.

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