Distribution of subclinical thyroid disease and other primary thyroid disorders in a tertiary care center

Shilpa HD^{1,*}, Nineetha Muraleedharan², Sulekha B³

¹Associate Professor, ²Assistant Professor, ³Professor, Dept. of Biochemistry, SUT Academy of Medical Sciences, Thiruvananthapuram

*Corresponding Author:

Email: shilpadhruva@gmail.com

Abstract

Background: Thyroid dysfunctions are common endocrine problems. They account for a considerable morbidity and mortality. Subclinical thyroid diseases especially subclinical hypothyroidism is a common clinical entity that encompass mild degree of thyroid dysfunction, clinical significance and management of which is still under study. (1) previous data show about half of the population with thyroid disease remain undiagnosed. (2) Thyroid disease may occur at any age and in both genders but its occurrence differs among geographical areas and in different age and sex groups. (3) Several studies are available about the distribution of thyroid diseases in west. However there are only limited Indian studies in this regard and there are variations in prevalence rates in different studies. (4) In one study from cochin prevalence of hypothyroidism and subclinical hypothyroidism were 3.9% and 9.4% respectively. (5) In other studies from Mumbai and Puducherry it was found to be 10.9% and 11.3% respectively. (6,7) Prevalence rates of subclinical hyperthyroidism and overt hyperthyroidism was 0.6% and 1.2% in one study and 1.6% and 1.3% respectively in another study. (5,6,7) Hence this study aims to find out the distribution of various thyroid disorders in the study population in this geographical area.

Materials and Methods: The study comprised of 164 subjects including 26 males and 138 females in the age group of 10-80 years. History and physical examination of the patients were carried out as per standard protocols. The thyroid profile i.e., TSH, T3, T4, fT3, fT4 was tested using ECLIA(electrochemiluminescence).

Results: It was found that primary hypothyroidism is 5 times more common in females than males. Primary hypothyroidism is 1.76 times common than primary hyperthyroidism. The occurrence of subclinical hypothyroidism is 11.58% and it is 18 times more common in females.

Conclusion: In this study it was found that the occurrence of subclinical hypothyroidism was quite high amounting to 11.58% and it was the highest in the female population. Among the other primary thyroid disorders, primary hypothyroidism was the commonest and exhibited female preponderance.

Keywords: Subclinical hypothyroidism, Primary hypothyroidism, Primary hyperthyroidism, TSH, T3, T4

Introduction

Thyroid dysfunction is one of the leading endocrine disorders. It represents 30-40% of patients seen in endocrine practice. (2) Subclinical thyroid disease affects 3-15% of the adult population. (7) The term subclinical thyroid disease describes conditions characterized by increase or decrease TSH levels in subclinical hypothyroidism and subclinical hyperthyroidism respectively with normal levels of circulating thyroid hormones with very few or no symptoms of thyroid disease. It is a diagnosis based on lab evaluation. Their importance lies in the possible adverse effects on heart, lipids, bone mineral density, quality of life and mortality. (8)

The normal thyroid gland controls the body metabolism, growth, development and maintains the internal milieu. Thyroid elaborates two key metabolic hormones T4 and T3. Both these hormones are under the control of TSH of anterior pituitary in turn controlled by thyrotropin releasing hormone(TRH) of the hypothalamus. Thyroid hormones are transported in plasma by proteins. Thyroxine binding globulin carries about 80% of T4 and 60% of T3. The bound form is biologically inactive. (9)

Primary thyroid disorders are due to diseases of the thyroid gland itself. Spectrum of thyroid disorders range from subclinical thyroid disease in which there are changes in TSH(increased subclinical in hypothyroidism and decreased in subclinical hyperthyroidism) with thyroid hormones in normal range to overt hypothyroidism in which the thyroid hormones (T3 and T4) are decreased and thyroid stimulating hormone (TSH) from the anterior pituitary is elevated, hyperthyroidism in which the thyroid hormones (T3,T4) are increased and TSH is decreased,(10,11) T3 thyrotoxicosis in which only T3 is elevated with T4 within normal range, (11) euthyroid sickness syndrome due to non thyroid illness as a result of adaptation to a new catabolic state and not due to thyroid disease itself. (11)

Even though it affects the entire population, more cases are reported from south east Asia, Latin America and central Africa. (14) The prevalence pattern of thyroid diseases depends largely on ethnicity, geography and environmental factors and iodine intake. It is different from other diseases in terms of ease of diagnosis and definitive treatment options. (15) The prevalence rate of subclinical thyroid disease has not been well studied in Indian scenario. Various studies have shown that

subclinical thyroid disease is associated with hyperlipidemia, neuromuscular and neuropsychiatric symptoms, myocardial dysfunction, progression to overt thyroid dysfunction.⁽⁷⁾ The necessisity for further evaluation, possible treatment and the urgency of treatment have not been clearly established.⁽¹⁶⁾

Previous studies have shown that occurrence of subclinical hypothyroidism is common than subclinical hyperthyroidism^(2,4) due to apparent asymptomatic nature the American Thyroid Association has recommended routine population screening of both sexes at age 35 yrs and then every 5 yrs for early detection and treatment of subclinical hypothyroidism.⁽⁷⁾

There is paucity in Indian data and there is no standard Indian guidelines for screening population for thyroid disorders. Different studies from India have reported different prevalence rates. In a study by Usha et al prevalence of hypothyroidism and subclinical hypothyroidism were 3.9% and 9.4% respectively. In other studies it was found to be 10.9% and 11.3% respectively. Prevalence rates of subclinical hypothyroidism and overt hyperthyroidism was 0.6% and 1.2% in one study and 1.6% and 1.3% respectively in another study. Hence this study aims to find out the distribution of various thyroid disorders in the study population in this geographical area to aid in the screening for thyroid diseases.

Materials and Methods

One hundred and sixty four subjects fulfilling the inclusion criteria were included in this cross sectional study

Inclusion criteria: All patients visiting the endocrinology division of our hospital with derangement of even single parameter in thyroid profile were selected.

Exclusion criteria: Previously diagnosed thyroid disorders, pregnant ladies, infants, history of intake of drugs one month prior to sampling, secondary thyroid disease were excluded.

Written informed consent was taken from all subjects and the study was approved by the institutional ethical committee.

Testing for thyroid hormones: 3-5ml of venous blood was collected, centrifuged as soon as the clot was formed and the serum was separated. Tests were done for TSH, T3. T4, fT3, fT4 using ECLIA(electro chemiluminescence) technology with vitrios immunoassay system.

Data Analysis: Data was analyzed to find out the frequency of various thyroid disorders and it was further segregated of age and sex .the relative frequencies and ratios were calculated for each group of disorders using SPSS software. Frequency bar charts and tables were prepared in Microsoft excel software program.

Results

Table 1 shows the distribution of thyroid disease among the study population. It can be seen that primary hypothyroidism is the most common thyroid disorder amounting to 54.88% and the occurrence of subclinical hypothyroidism is 11.58%.primary hyperthyroidism amounts to 31.09%, subclinical hyperthyroidism is 1.82%, T3 toxicosis 0.6%. Table 2 shows the age wise distribution of thyroid disease. The occurrence of thyroid diseases is most common in age group of 16-40yrs (55.48%) primary hypothyroidism (29.87%), hyperthyroidism 17.07%, primary subclinical hypothyroidism 7.32%, subclinical hyperthyroidism 1.22%. Among the age group of >40 yrs occurrence of thyroid diseases amounts to 42.68%. Primary hypothyroidism is the most commonest which is 23.78%, subclinical hypothyroidism amounts to 4.27%, hyperthyroidism is 13.41% primary and thyrotoxicosis & subclinical hyperthyroidism was found in only one patient >40 yrs (0.61%). Among the younger age group(1-15yrs) the occurrence of thyroid diseases was 1.83%, of which primary hypothyroidism was 1.22% and no cases of subclinical thyroid disease reported in this age group. hyperthyroidism was seen in only 1 patient (0.61%) in 1-15 yrs age group. Table 3 shows gender wise distribution of thyroid disorders. It is seen that the occurrence of thyroid diseases is more common among females (84.15%), of which 45.73% amounts to primary hypothyroidism, subclinical hypothyroidism is 10.98%, subclinical hyperthyroidism 1.83%, primary hyperthyroidism is 25%, T3 toxicities was seen in one patient (0.61%). Among males (occurrence of thyroid disease---15.84%) primary hypothyroidism commonest i.e., 9.14%. subclinical hypothyroidism was male(0.61%),found in only one hyperthyroidism 6.09%. no cases of subclinical hyperthyroidism and T3 toxicosis were reported.

Table 4 shows the ratio of thyroid disorders among study population. The ratio of primary hypothyroidism to primary hyperthyroidism is 1.8:1. Among males, it was 1.5:1 and among females it was 1.8:1. The ratio of subclinical hypothyroidism to subclinical hyperthyroidism was 6.3:1. Among males it was 1:0 and among females, 6:1. The ratio of subclinical hypothyroidism to primary hypothyroidism was 1: 4.7 in general population.

Table 5 shows female to male ratio of thyroid diseases. For primary hypothyroidism, it was 5:1, for primary hyperthyroidism it was 4.1:1. Subclinical hypothyroidism 18:1, subclinical hyperthyroidism 3:0.

Table 6 & 7 shows age wise distribution of thyroid diseases in males and females. It is seen that the pattern is almost similar with primary hypothyroidism being the most common disorder and in the age group 16 to 40. Subclinical hypothyroidism is also common in 16-40 year age group in both men and women and is common in female population. Table 8 shows the mean

and standard deviation of thyroid function tests in various thyroid disorders.

Table 1: Distribution of thyroid disease among study population

population								
Thyroid Diseases	Frequency	Percentage(%)						
Primary hypothyroidism	90	54.88						
Primary	51	31.09						
hyperthyroidism								
Subclinical	19	11.58						
hypothyroidism								
Subclinical	3	1.82						
hyperthyroidism								
T3 toxicosis	1	0.6						
Total	164	100						

Table 2: Age wise distribution of thyroid disease among study population

Age Group	1-15 Yea	rs	16-40 Ye	ars	> 40 Years		
Thyroid disease	Frequency	% †	Frequency	%	Frequency	%	
Primary hypothyroidism	2	1.22	49	29.87	39	23.78	
Primary hyperthyroidism	1	0.61	28	17.07	22	13.41	
Subclinical hypothyroidism	0	0	12	7.32	7	4.27	
Subclinical hyperthyroidism	0	0	2	1.22	1	0.61	
T3 toxicosis	0	0	0	0	1	0.61	
Total	3	1.83	91	55.48	70	42.68	

[†] Percentage of thyroid disease among total study population(N= 164).

Table 3: Gender wise distribution thyroid disease among study population

Gender	Male	Male		le
Thyroid disease	Frequency	% [‡]	Frequency	%
Primary hypothyroidism	15	9.14	75	45.73
Primary hyperthyroidism	10	6.09	41	25
Subclinical hypothyroidism	1	0.61	18	10.98
Subclinical hyperthyroidism	0	0	3	1.83
T3 toxicosis	0	0	1	0.61
Total	26	15.84	138	84.15

[‡] Percentage of thyroid disease among total study population(N= 164).

Table 4: Ratio of thyroid disorders among study population

Tuble it ituite of mytoid disorders among study population								
Ratio	Total	Males	Females					
	Population	(Total=26)	(Total=138)					
Primary hypothyroidism: Primary hyperthyroidism	1.8:1	1.5 : 1	1.8:1					
Subclinical hypothyroidism: Subclinical hyperthyroidism	6.3 : 1	1:0	6:1					
Subclinical hypothyroidism: Primary hypothyroidism	1:4.7	1:15	1:4.2					

Table 5: Ratio of females to males with thyroid disorder

Ratio	Female : Male
Primary hypothyroidism	5:1
Primary hyperthyroidism	4.1 : 1
Subclinical hypothyroidism	18:1
Subclinical hyperthyroidism	3:0

Table 6: Agewise distribution of thyroid diseases among males

Thyroid disease	1-15 Years		16-40 Years		> 40 Ye	ars	Tota	ıl
	Frequency	%*	Frequency	%	Frequency	%	Frequency	%
Primary	2	7.69	8	30.77	5	19.23	15	57.69%
hypothyroidism								
Primary	0	0	6	23.08	4	15.38	10	38.46%
hyperthyroidism								
Subclinical	0	0	1	3.85	0	0	1	3.85%
hypothyroidism								
Subclinical	0	0	0	0	0	0	0	0
hyperthyroidism								
T3 toxicosis	0	0	0	0	0	0	0	0
Total	2	7.69	15	57.69	9	34.61	26	100%

^{*}percentage distribution among males

Table 7: Age wise distribution of thyroid diseases among females

Thyroid disease	1-15 Years		16-40 Years		> 40 Ye	ars	Total	
	Frequency	%**	Frequency	%	Frequency	%	Frequency	%
Primary	0	0	41	29.71	34	24.64	75	54.35
hypothyroidism								
Primary	1	0.72	22	15.94	18	13.04	41	29.71
hyperthyroidism								
Subclinical	0	0	11	7.97	7	5.07	18	13.04
hypothyroidism								
Subclinical	0	0	2	1.45	1	0.72	3	2.17
hyperthyroidism								
T3 toxicosis	0	0	0	0	1	0.72	1	0.72
Total	1	0.72	76	55.07	61	44.2	138	100

^{**}percentage distribution among females

Table 8: Mean and Standard Deviation of TFT values

	Tuble of fredh and Standard Deviation of 111 values							
	TSH	Т3	T4	fT3	fT4			
	(0.465-	(0.97-	(5.53-	(4.26-	(10-			
	4.68mIU/mL)*	1.69ng/mL)	11µg/dL)	8.10pmol/L)	28.2pmol/L)			
Primary	9.27±4.95	0.68±0.14	3.31±0.9	3.7±0.16	7.47±0.85			
Hypothyroidism								
Primary	0.147±0.13	1.83 ± 0.67	14.23 ±3.4	9.7 ± 0.57	33.01 ±2.27			
Hyperthyroidism								
Subclinical	6.19 ± 0.95	1.4 ± 0.82	8.9 ± 0.76	6.23 ± 0.32	12.46 ± 0.92			
Hypothyroidism								
Subclinical	0.307 ± 0.07	1.02 ± 0.56	8.09 ± 1.22	6.2 ± 0.32	16.6 ±1.28			
Hyperthyroidism								

^{*}normal range

Discussion

In the present study it was found that the occurrence of subclinical hypothyroidism was quite high in the study population amounting to 11.58% which is in agreement with the study by Deshmukh et al⁽⁷⁾ (prevalence-11.3%) and subclinical hyperthyroidism was 1.82% while Usha et al reported it to be 0.6%.⁽⁵⁾ Further, it was found that subclinical thyroid diseases is much more predominant among females than in males. Subclinical hypothyroidism is 18 times more common in females than males and subclinical hyperthyroidism was found only in

females(total number 3 out of 164)in the study population. The estimated prevalence of subclinical hypothyroidism world-wide ranges from 1-10%.⁽¹⁷⁾ The occurrence of subclinical thyroid disease was more common in females compared to males in the present study which is accordance with other studies.⁽¹⁸⁾ Our study showed higher prevalence rates of subclinical hypothyroidism than other studies.^(7,19)

Subclinical hypothyroidism can be found in areas with excessive iodine intake and the most common cause is autoimmunity. The clinical importance and treatment of mild TSH elevation (TSH<10mIU/L)

remains subject of debate. Increased prevalence of subclinical hypothyroidism is associated with risk factors like hyperlipidemia, neurological and metabolic derangements. Regression to overt hypothyroidism increases with presence of anti TPO(thyroperoxidase) antibodies and high TSH values. (20) In this setting of high rates of occurrence of subclinical thyroid disease and its associated complications, screening for thyroid diseases should be considered and there is a need for the establishment of national screening guidelines for the same.

Among other primary disorders occurrence of hypothyroidism was commoner accounting to 54.8% and it also showed a female preponderance with female to male ratio being 5:1 and in the age group of 16-40 yrs which is accordance with other studies. (21,22) The maximum number of subjects with thyroid disease fall in the age group of 16-40yrs which is contrary to the understanding that thyroid disorders occur in older age and increase with age. (23) T3 thyrotoxicosis was found in only one 41 year old female patient.

Conclusions

Among the overt primary thyroid disorders it was found that the occurrence of primary hypothyroidism was 54.8% and hyperthyroidism was 31.09% and was more common in females. Thyroid disorders were found to be relatively less in younger population (1-15yrs) and most common in 16-40 year age group in the present study with female preponderance.

The occurrence of subclinical hypothyroidism was found to be quite high (11.58%), subclinical hyperthyroidism was 1.82%. Subclinical thyroid disease is associated with various somatic and psychological derangements and it may progress to overt thyroid disease. Hence proper screening guidelines should be established to aid in the early diagnosis and management of this disorder.

References

- DS Cooper, B Biondi. Subclinical thyroid disease. Lancet.2012 Mar;379(9821);1142-1154.
- MA Garmendia, Palacios SS, Guillen-Gima F, Juan C, Galfore. The incidence and prevalence of thyroid dysfunction in Europe: A metaanalysis. J Clin Endocrinol Metab.2014 Mar;99(3):923-31.
- Hedinger C. Geographic pathology of thyroid diseases. Pathol Res Pract. 1981 May; 171(3-4):285-92.
- Unnikrishnan AG, Menon UV. Thyroid disorders in India; An epidemiological perspective. Indian J Of Endocrinol Metab 2011;1592:78-81.
- Usha MV, Sundaran KR, Unnikrishnan AG, Jayakumar RV, Nair V, Kumar H. Prevalence of undetected thyrois disorders in an iodine sufficient adult south Indian population. J. Indian Med Assoc. 2009;107:72-77.

- Unnikrishnan AG, Kalra S, Sahay RK, Bantwal G, John M, Tewari N. Prevalence of hypothyroidism in adults. An epidemiological study in eight cities in India. Indian J Endocrinol Meatb. 2013 July-August; 17(9);647-652.
- Deshmukh V, Behl A, Iyer V, Joshi H, Dhoyle JP, Varthakavi PK. Prevalence, clinical, and biochemical profile of subclinical hypothyroidism in normal population in Mumbai. Indian J Endocrinol Metab. 2013 May;17(3):454-9.
- Burgio A, Gruttadaeria G, Fulco G, Lunetta MC, Vancliri F. Subclinical thyroid diseases. Recenti Prog Med2005;96(7-8):382-91.
- Thomas J, Schmidt, Litwack G. Biochemistry of hormones. In: Thomas M Devlin editor. Text book of biochemistry with clinical correlations. 6th ed. Wiley-liss. 2006.p892-943.
- Philips JA. Throid hormone disorder/released May 2001.Available from: http://www.csa.com/discovery guides/thyroid/overview.php.
- Larsen PR, Davies TF, Hay ID. The thyroid.in: Williams Wilson JD, Foster DW, Kronberg HM, editors. Williams Text Book of Endocrinology. 9th ed.Philadelphia:Saunders;1988.p.389-416.
- 12. Konardy A, Oszlatly B, Reszleg I, Korhaz Jo.T3 throtoxicosis incidence, significance and connection with iodine intake. ORV hetil. 2000 Feb 13;141(7):337-40.
- Krohn K, Fuhrer D, Bayer Y, Eszlinger M, Braurer V, Neumann S et al. Molecular pahtrogenesis of euthyroid and toxic multinodular goiter. Endocrine rev. June:2005;26(4):504-524.
- Vanderpump MP. The Epidemiology of thyroid diseases.in: Breveman LE, Utiger RD, editors. Wesner ans Ingbars The Thyroid: A fundamental and clinical Text. 9th ed. philadelphia: JB lippincot-Raven;2005.p 398-496.
- Antony j, TM Celine, Chacko M. Spectrum of thyroid disorders: A retrospective study at a medical college hospital. Thyroid research and practice. 2014 Mar. 11(2)p 55-59.
- Surks MI, Ortiz E, Daniel GH, Sawin CT, Col NF, Cobin Rh et al. Subclinical thyroid disease: scientific review and guidelines for diagnosis and management. JAMA.2004 Jan;291(2):228-38.
- Cooper DS. Subclinical hypothyroidism. N. Eng T:Med July 26.2000:354(4)260-265.
- Araham R, Murugan VS, Pukazhavanthen P, Sen SK. Thyroid disorders of women of Puduchery. Ind J Clin Biochem. 2009:24(1)52-59.
- Tunbridge WM, Evered DC, Hall R, Appleton D, Brewis M, Clark F et al. The spectrum of thyroid disease in a community: The Whickhan survey. Clin Endocrinol (oxf). 1977 dec;7(6):481-93.
- Fatourechi V. Subclinical hypothyroidism: an update for primary care physician: Mayo clin Proc.2009 Jan;84(1):65-71.
- Saha PK, Baur B, Gupta S. Thyroid stimulating hormone measurement as the confirmatory diagnosis of hypothyroidism. A study from tertiary care teaching hospital, Kolkata. Ind J Comm Med 2007;32(2):139-140.
- 22. Vanderpump MP, Turnbridge WM. Epidemiology and prevention of clinical and subclinical hypothyroidism. thyroid2002;12:839-47.
- 23. Gersing A, Lewinski A, Lewinska MK. The thyroid gland and the process of ageing; what is new? Thyroid Research 2012;5:16.