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Research Article

DETECTION OF UNDIAGNOSED THYROID DISEASE IN PATIENTS MORE THAN 50 YEARS AND ABOVE

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ABSTRACT

Prevalance of thyroid disorders increases as age progresses [1]. They are challenging to diagnose due to atypical presentation and wide variety of co morbid conditions. Undiagnosed thyroid dysfunction can be associated with significant morbidity as age increases. **Objective:** To detect undiagnosed thyroid disease in patients age 50 years and above. **Methods:** The study included 300 subjects (both in patient and outpatient department), age 50 years and above attending Department of medicine at tertiary hospital New Delhi. The Out-patient subjects were asked to return on another day after 10-hour fast for determination of Serum Thyroid stimulating hormone, Free Triiodothyronine, Free Tetraiodothyronine, Anti-thyroperoxidase antibody levels. **Results:** Total of 300 subjects (males-171, females-129), aged between 50-93 (Mean 62.78 SD: 9) years, were included in the study. Although abnormal thyroid functions were present in 62% of the subjects, definite thyroid disease was present in 15.67%. Amongst 15.67%, hypothyroid and hyperthyroid state was present in 12.67%, and 3% respectively. Prevalence of thyroid disorder was higher in males (16.68%) than females (14.73%). Hyperthyroid state was common in males (3.51%) whereas hypothyroid state was equally common in both males (12.87%) and females (12.40%). Subclinical hypothyroidism (10.67%) was commoner than overt hypothyroidism (2%) amongst those with hypothyroidism. Hyperthyroid state was prevalent in (3%) subjects of which (0.33%) were overt hyperthyroid and (2.67%) had subclinical hyperthyroidism. Anti TPO antibodies were common in hypothyroid state (31.58%) than hyperthyroid (22.22%) state. **Conclusion:** A strong clinical suspicion of thyroid disease must be considered in elderly patients who present with vague symptoms like generalised weakness, easy fatigability, lethargy and disinterest in daily activities. Therefore patients more than 50 years and above must be screened for abnormal thyroid function.

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INTRODUCTION

Prevalance of thyroid disorders increases as age progresses [1]. They pose a diagnostic challenge owing to atypical presentation associated co morbid conditions. Further interpretation of thyroid function tests can often be misleading due to accompanying co morbidities and drugs that may interfere with thyroid function.

As age advances, the thyroid gland undergo progressive fibrosis [2] and prevalence of auto antibodies also increases, reaching up to 20% in women with age 60 years and above [3]. Also symptoms related to abnormal thyroid function are subtle or even absent, and can be often mistaken as age related changes. Hence thyroid disease may be overlooked or even misdiagnosed [4], which makes things more difficult for a clinician regarding decision to treat. Therefore diagnosis of

thyroid disease in elderly requires a high index of suspicion. There is a paucity of literature from India regarding undiagnosed thyroid disease in patients aged 50 years and above. Problem is compounded by the fact that India does not ask for routine screening for thyroid disease unlike some of the developed countries.

OBJECTIVES

Primary objective

Identifying undiagnosed thyroid disease in patients age 50 years and above in both In-Patients and Out-patients.

Secondary objective

To sub-classify diagnosed thyroid function as hypothyroid, euthyroid, and hyperthyroid to enable treatment decision.

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MATERIALS AND METHODS

An institution based cross sectional analytical study was conducted from November 2018- March 2020 in the Department of Medicine and Biochemistry at tertiary hospital. A total of 300 subjects (both in patient and out patient department) aged 50 years and above were enrolled in the study after an informed consent with the following inclusion and exclusion criteria.

Inclusion criteria

In-patients and Outpatients age 50 years and above, with no previous history of thyroid disease, head and neck surgery or treatment for head and neck cancers.

Exclusion criteria

1. Diagnosed thyroid illness and/or history of treatment (medical, surgical, nuclear, or radiation therapy) for thyroid illness.
2. History of surgery or radiation of the thyroid for non-thyroid related illness (e.g. laryngeal cancer).
3. Diagnosed pituitary disease and/or history of pituitary surgery.
4. Intake of medications known to affect thyroid hormone levels (e.g. amiodarone, antipsychotics).

The Out-patient subjects were asked to return on another day after a 10-hour fast for determination of Serum Thyroid stimulating hormone (TSH), Free Triiodothyronine (FT3), Free Tetraiodothyronine (FT4), Anti-thyroperoxidase antibody levels (Anti TPO Ab) .

All patients included in the study were subjected to FT3, FT4, TSH, Anti Thyroperoxidase Antibody. Samples were processed on FULLY AUTOMATED CHEMILUMINESCENCE based analyser Beckman Dxi model.

STATISTICAL ANALYSIS

Categorical variables were presented as number and percentage (%) and continuous variables were presented as mean ± SD and median. Qualitative variables were analyzed using Chi-Square test/Fisher’s Exact test. A p value of <0.05 was considered statistically significant. The data was entered in MS EXCEL spreadsheet and analyzed was done using Statistical Package for Social Sciences (SPSS) version 21.0.

OBSERVATIONS AND RESULTS

A total of 300 subjects aged between (50-93) years were evaluated. Mean age was 62.78 (± 9 years). Majority of subjects 66 (22%) were in the age group of 60-64 years. Out of 300 cases 171 (57%) were males and 129 (43%) were females. Abnormal thyroid function was present in (15.67%), of which hypothyroid state and hyperthyroid state was present in 12.67%, 3% respectively (table 1). A substantial number of subjects with abnormal thyroid functions 139 (46%) could not be categorized into any of the defined sub-clinical or clinical state of thyroid disease, due to isolated changes in FT3, FT4 or Anti-TPO antibodies. Out of 38 subjects with hypothyroidism, 32 (10.67%) subjects were in a subclinical hypothyroid state and 6 (2%) had an overtly hypothyroid state. Out of 9 subjects in hyperthyroid state one was overtly hyperthyroid and 8 (2.67%) subjects had a subclinical hyperthyroid state.

Table 1 Distribution of thyroid function of study subjects.

Thyroid function	Frequency	Percentage
Euthyroid	114	38.00%
Hypothyroid	38	12.67%
Overt hypothyroid	6	2.00%
Subclinical hypothyroid	32	10.67%
Hyperthyroid	9	3.00%
Overt hyperthyroid	1	0.33%
Subclinical hyperthyroid	8	2.67%
Unclassified	139	46.33%
Isolated increase in FT3 with low TSH	2	0.67%
Isolated increase in FT4 with low TSH	3	1.00%
Isolated decrease in FT3 /FT4 ±TPO antibodies	67	22.33%
Isolated TPO ab (antibody) positivity	11	3.67%
Unexplained abnormal thyroid functions	56	18.67%

FT3: Free Triiodothyronine; FT4: Tetraiodothyronine; TSH, Thyroid stimulating hormone
TPO ab: thyroperoxidase antibody.

Hyperthyroidism was common in males (3.51%) and hypothyroidism was equally common in both males (12.87%) and females (12.40%). Majority of subjects with hypothyroidism were in the age group 50-54years (22.41%) and hyperthyroidism in age group 75 years and above.

In the study lethargy was the most common symptom. Out of 126 subjects who had lethargy, 46 (40.35%) were euthyroid, 17 (44.74%) were hypothyroid, 5 (55.56%) were in hyperthyroid state. Substantial number of 58 subjects (41.73%) were in unclassified group. Statistical association of most symptoms with thyroid disorder was insignificant (p>0.05) except cold intolerance (p = 0.001) and loose stools (p=0.015).

Dry skin was the most common sign. Out of 126 subjects with dry skin 39 (34.21%) were euthyroid, 19 (50%) were hypothyroid, 5 (55.56%) were hyperthyroid and 63 (45.32%) were in unclassified group. The statistical association of clinical signs with type of thyroid disorders was found to be statistically insignificant (p>0.05) except pretibial edema (p= 0.01).

The frequency of TPO antibodies positivity in hypothyroid, hyperthyroid, and unclassified state was 31.58% , 22.22%, and 24.46% respectively. 4(66.67%) subjects with overt hypothyroid state and 8(25%) subjects with subclinical hypothyroid state had positive TPO antibodies. The TPO antibodies were positive in the only subject in overt hyperthyroid state and 12.50% of those in a subclinical hyperthyroid state. The association of various parameters with thyroid profile is depicted in table 2.

Table 2 Association of various variables with thyroid profile

Parameters		Euthyroid	Hypothyroid	Hyperthyroid	Unclassified	Total	P value	Test performed
		(n=114)	(n=38)	(n=9)	(n=139)			
Gender								
Female		46 (35.66%)	16 (12.40%)	3 (2.33%)	64 (49.61%)	129 (100%)	0.751	Chi square test, 1.207
Male		68 (39.77%)	22 (12.87%)	6 (3.51%)	75 (46.83%)	171 (100%)		
Symptoms								
Weight gain	Absent	105 (92.11%)	37 (97.37%)	8 (88.89%)	124 (89.21%)	274 (91.33%)	0.441	2.695
	Present	9 (7.89%)	1 (2.63%)	1 (11.11%)	15 (10.79%)	26 (8.67%)		
Weight loss	Absent	101 (88.60%)	36 (94.74%)	9 (100%)	123 (88.49%)	269 (89.67%)	0.486	2.44
	Present	13 (11.40%)	2 (5.26%)	0 (0%)	16 (11.51%)	31 (10.33%)		
Heat intolerance	Absent	112 (98.25%)	37 (97.37%)	8 (88.89%)	138 (99.28%)	295 (98.33%)	0.118	5.881
	Present	2 (1.75%)	1 (2.63%)	1 (11.11%)	1 (0.72%)	5 (1.67%)		
Cold intolerance	Absent	113 (99.12%)	38 (100%)	8 (88.89%)	139 (100%)	298 (99.33%)	0.001	16.09
	Present	1 (0.88%)	0 (0%)	1 (11.11%)	0 (0%)	2 (0.67%)		
Hair loss	Absent	95 (83.33%)	30 (78.95%)	6 (66.67%)	112 (80.58%)	243 (81%)	0.631	1.725
	Present	19 (16.67%)	8 (21.05%)	3 (33.33%)	27 (19.42%)	57 (19%)		
Loose stools	Absent	110 (96.49%)	38 (100%)	9 (100%)	123 (88.49%)	280 (93.33%)	0.015	10.426
	Present	4 (3.51%)	0 (0%)	0 (0%)	16 (11.51%)	20 (6.67%)		
Constipation	Absent	98 (85.96%)	34 (89.47%)	8 (88.89%)	116 (83.45%)	256 (85.33%)	0.792	1.04
	Present	16 (14.04%)	4 (10.53%)	1 (11.11%)	23 (16.55%)	44 (14.67%)		
Palpitations	Absent	101 (88.60%)	34 (89.47%)	7 (77.78%)	127 (91.37%)	269 (89.67%)	0.583	0.949
	Present	13 (11.40%)	4 (10.53%)	2 (22.22%)	12 (8.63%)	31 (10.33%)		
Lethargy	Absent	68 (59.65%)	21 (55.26%)	4 (44.44%)	81 (58.27%)	174 (58%)	0.819	0.927
	Present	46 (40.35%)	17 (44.74%)	5 (55.56%)	58 (41.73%)	126 (42%)		
Voice change	Absent	106 (92.98%)	37 (97.37%)	8 (88.89%)	136 (97.84%)	287 (95.67%)	0.185	4.83
	Present	8 (7.02%)	1 (2.63%)	1 (11.11%)	3 (2.16%)	13 (4.33%)		
Goitre	Absent	112 (98.25%)	36 (94.74%)	8 (88.89%)	136 (97.84%)	292 (97.33%)	0.265	3.964
	Present	2 (1.75%)	2 (5.26%)	1 (11.11%)	3 (2.16%)	8 (2.67%)		
Eye signs	Absent	112 (98.25%)	37 (97.37%)	8 (88.89%)	135 (97.12%)	292 (97.33%)	0.413	2.862
	Present	2 (1.75%)	1 (2.63%)	1 (11.11%)	4 (2.88%)	8 (2.67%)		
Dry skin	Absent	75 (65.79%)	19 (50%)	4 (44.44%)	76 (54.68%)	174 (58%)	0.161	5.147
	Present	39 (34.21%)	19 (50%)	5 (55.56%)	63 (45.32%)	126 (42%)		
Hair loss	Absent	80 (70.18%)	28 (73.68%)	6 (66.67%)	101 (72.66%)	215 (71.67%)	0.944	0.38
	Present	34 (29.82%)	10 (26.32%)	3 (33.33%)	38 (27.34%)	85 (28.33%)		
Eye/facial puffiness	Absent	89 (78.07%)	26 (68.42%)	7 (77.78%)	98 (70.50%)	220 (73.33%)	0.487	2.437
	Present	25 (21.93%)	12 (31.58%)	2 (22.22%)	41 (29.50%)	80 (26.67%)		
Hoarseness	Absent	111 (97.37%)	36 (94.74%)	9 (100%)	134 (96.40%)	290 (96.67%)	0.812	0.954
	Present	3 (2.63%)	2 (5.26%)	0 (0%)	5 (3.60%)	10 (3.33%)		
Tremors	Absent	107 (93.86%)	34 (89.47%)	8 (88.89%)	119 (85.61%)	268 (89.33%)	0.215	4.474
	Present	7 (6.14%)	4 (10.53%)	1 (11.11%)	20 (14.39%)	32 (10.67%)		
Clubbing	Absent	111 (97.37%)	35 (92.11%)	9 (100%)	130 (93.53%)	285 (95%)	0.372	3.127
	Present	3 (2.63%)	3 (7.89%)	0 (0%)	9 (6.47%)	15 (5%)		
Pretibial edema	Absent	113 (99.12%)	35 (92.11%)	7 (77.78%)	131 (94.24%)	286 (95.33%)	0.011	11.175
	Present	1 (0.88%)	3 (7.89%)	2 (22.22%)	8 (5.76%)	14 (4.67%)		
TPO antibodies								
TPO antibodies	Normal	114	26	7	105	252	<0.0001	36.239
		(100%)	(68.42%)	(77.78%)	(75.54%)	(84%)		
	High	0	12	2	34	48		
		(0%)	(31.58%)	(22.22%)	(24.46%)	(16%)		
Total	114	38	9	139	300			
	(100%)	(100%)	(100%)	(100%)	(100%)			

DISCUSSION

The present study was conducted in the Department of Medicine and Biochemistry at tertiary hospital, New Delhi, India. Limited literature is available regarding prevalence of thyroid disease in elderly from North India. Most of the studies related to thyroid disorder in India are conducted in subjects aged 60 years and above. However, the present study was conducted in subjects 50 years or more in age with majority of the subjects in the age group of 60-64 years as the life expectancy in India is lower.

In the present study thyroid disease was present in (15.67 %), Amongst those with abnormal thyroid function, hypothyroid and hyperthyroid state was present in (12.67%) and (3%) respectively. This was in accordance to the study done in

Kerala by Dr Laxminarayan GR et. al [5], where the frequency of thyroid disease was (13.9%)

Among the unclassified 139 (46%) subjects, half of the subjects 67 (22.33%) were found to have an isolated decrease in either FT3 or FT4 with or without presence of TPO antibodies. Such patients with unexplained abnormal of thyroid functions must be re-evaluated periodically before overt hypothyroid or hyperthyroid state manifests.

In the present study different types of thyroid disorder were common in different age group. However, association between thyroid disease and age was statistically insignificant (p = 0.115).Hence thyroid diseases are common in elderly irrespective of age.

Thyroid disease was common in males (16.68%) than females (14.73%). Amongst the thyroid abnormalities, hypothyroidism was the commonest abnormality (12.67%) which was in conformity to the study conducted in Kerala (10%) in 2017 and Karnataka 2019 (22%). Also the study conducted by Dr Madhuvan et al [6] from Bangalore showed that hypothyroidism (20%) was common than hyperthyroidism.

Amongst the hypothyroid subjects, frequency of subclinical hypothyroid state was common (10.67%) than overt hypothyroid state (2%). This was in conformity to study conducted by Dr Neelakshi Mahanta et al [7] in Assam in September 2017, which showed a higher frequency of subclinical hypothyroidism (25%) as compared to overt hypothyroidism. In the study, subclinical hyperthyroid state (2.67%) was common as compared to overt state (0.33%). This was in agreement with the study done by Natasha et al [8] in Karnataka in which the subclinical hyperthyroid state (14.28%) was common than overt hyperthyroid state (7.14%). However, the association between hypothyroid disease state and gender was $p=0.751$. Hence the hypothyroid state is common in elderly irrespective of gender.

In the present study, lethargy (42%) was the commonest symptom followed by hair loss (19%) among the study subjects. However, studies from Karnataka, Bangalore and Assam reported easy fatigability and generalized weakness as the most common symptom. These symptoms however are likely to be present in patients with age 50 years and above, and are therefore non-specific. The study found no association between symptoms and thyroid disorder ($p > 0.05$) except for cold intolerance ($p = 0.001$) and loose stools ($p = 0.015$).

Lethargy despite being the most common symptom was not reported by nearby 174 subjects, but on biochemical evaluation, 21 of these subjects had hypothyroid state and 4 had hyperthyroid state. Although 68 were still biochemically euthyroid and 81 could not be classified. This was noted with all the symptoms. Therefore, it is important to screen all asymptomatic subjects 50 years and above for thyroid disease. There were a substantial number of subjects who did not report any symptom but on screening were found to have abnormal thyroid function. These findings suggest that thyroid disease cannot be predicted only from clinical symptoms alone in the elderly. Further it may not be necessary for thyroid disease to present with symptoms in elder patients with age 50 years and above.

In the study anti TPO antibodies were found in 48 subjects (16%). The anti-TPO antibodies were more common in hypothyroid state (31.58%) than in hyperthyroid state (22.22%). Among the hypothyroid subjects, anti-TPO antibodies were common in the overt state (66.67%) as compared to subclinical hypothyroid state (25%). This was in conformity to the study done in Bangalore which also reported similar data. The anti TPO antibodies were positive in one patient with overtly hyperthyroid state in which the association was statistically significant.

Patients may remain asymptomatic for years before being diagnosed with an overt thyroid disease and/or its complications.

It is often difficult for a physician to suspect thyroid disease just on the basis of symptoms, therefore biochemical evaluation is also needed to confirm the disease. Considering the fact that generalized weakness and fatigue is the most common clinical presentation in thyroid disease, any elderly patient with such presentation must be evaluated for thyroid disease. It is definite that co-morbidities along with age related changes makes it difficult to clinically suspect thyroid disease. Not many papers have been published in India comparing clinical features of thyroid disorders in this wide range of age group. This study may throw some light on the subject. However the study was conducted only in the department of medicine of single institution with small hospital based sample size. Therefore data cannot be extrapolated to the general population.

CONCLUSION

The present study was designed to estimate the frequency of undiagnosed thyroid disease in subjects 50 years and above. Clinical presentation of abnormal thyroid function in elderly is different from that of subjects from younger age group. Since there was no association of abnormal thyroid functions with age, gender and symptoms, any patient of age 50 years and above presenting to a general physician must be evaluated for thyroid disease irrespective of gender and symptoms and age. This would enable us to diagnose a substantial number of subjects who would benefit from treatment.

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