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A study on thyroid dysfunction and lipid profile in postmenopausal women

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Abstract
Aims and Objectives
1. To study the prevalence of thyroid dysfunction in postmenopausal women.
2. To study the effects of thyroid dysfunction on lipid profile.

Material and Methods: One hundred postmenopausal women attending the outpatient and inpatients of Medicine department in NRI medical college were randomnly selected and included in this cross sectional study. The patients were examined for clinical features of thyroid dysfunction and screened for the presence of thyroid dysfunction. The thyroid dysfunction was correlated with dyslipidemia and presence of ischaemic heart disease.

Results: Prevalence of subclinical hypothyroidism was found to be 22%, of clinical hypothyroidism was 8% and of thyrotoxicosis was 2%. It was seen that thyroid dysfunction prevalence increased with increasing age. It was seen that thyroid dysfunction has a correlation with duration of menopause with maximum patients having more than 10 years of menopause. There was a significant correlation between thyroid dysfunction and BMI. Maximum patients with thyroid dysfunction were overweight or had grade 1 obesity.

Dyslipidemia was found to be statistically associated with thyroid dysfunction with a P value of 0.014. 38.9% of Subclinical hypothyroidism and 8.3% of clinical hypothyroid patients were found to have dyslipidemia. Predominant pattern of dyslipidemia seen was hypercholesterolemia. The presence of IHD was not statistically associated with thyroid dysfunction, in our study.

Conclusion: Hence screening can be recommended for hypothyroidism in postmenopausal women especially in those with increasing age, duration of menopause and overweight, to evaluate and correct dyslipidemia so as to prevent adverse artherosclerotic cardiovascular complication.

Keywords: dyslipidemia, postmenopausal, hypothyroidism, atheroscelrosis, coronary heart disease

Introduction

Thyroid disorders are common disorders of general population, more common in females [1]. Thyroid dysfunction may be in the form of increased (Hyperthyroidism/Thyrotoxicosis) or decreased (Hypothyroidism) function, it may be subclinical or overt.

Hypothyroidism is a common thyroid disorder and is more common in elderly women [2]. Subclinical is more common than overt hypothyroidism. It is usually autoimmune in origin presenting as Hashimoto's thyroiditis or as atrophic thyroiditis [1]. In contrast Hyperthyriodism is less common than hypothyroidism. In hyperthyroidism Graves disease is most common, mainly affecting young adults and Toxic multinodular goitre is less common mainly affecting older age group [1].

Thyroid dysfunction, mainly hypothyroidism affects almost all systems of body. It affects skin with its appendages, cardiovascular, respiratory, alimentary, central and peripheral nervous system, musculoskeletal and endocrinal systems [1]. In energy metabolism dysfunction it causes reduction in glucose disposal to skeletal muscle and adipose tissue. It also affects lipid metabolism by depressing both synthesis and degradation of lipids leading to accumulation of low density lipids and Triglycerides [3, 4, 5, 6].

Postmenopause is the period of time after menopause. Menopause is diagnosed retrospectively, as twelve consecutive months of amenorrhoea, due to loss of ovarian follicular function. There occurs dramatic hormonal changes [7]. There is fall in reproductive hormones like progesterone, estradiol and rise in FSH, LH. Therefore there is loss of beneficial effects of reproductive hormones, example, loss of beneficial effect of estrogen on lipid metabolism, which causes increase in low density lipids and decrease in high density

lipids. Therefore postmenopause is a state of increased cardiovascular risk mainly due to dyslipidemia.

Postmenopausal women have increased risk of developing Hypothyroidism [2] which may be subclinical or overt. One important reason being autoimmunity which develops easily with age including autoimmune thyroid disease [2]. This further adds to cardiovascular risk due to dyslipidemia and increases risk of IHD and stroke [4, 5, 6].

According to the American Association of Clinical Endocrinologists (AACE), millions of women with unresolved menopausal like symptoms may be suffering from undiagnosed thyroid disease. While symptoms such as fatigue, depression, mood swings and sleep disturbances are frequently associated with menopause. They may also be signs of hypothyroidism. Overt thyroid dysfunction was found to be present in 1 in 71 women of over 60 years of age. The prevalence of overt hypothyroidism was found to be 2% in these women. As women spend one third of their lives after menopause, screening can effectively detect the presence of thyroid dysfunction in postmenopausal women and has been recommended [8].

Objectives of study

1. To study the prevalence of thyroid dysfunction in postmenopausal women.
2. To study the effects of thyroid dysfunction on lipid profile.

Material and Methods

Source of Data

Postmenopausal women who fulfil the inclusion and exclusion criteria as mentioned below, attending the outpatient and inpatient of Medicine department in NRI Medical College Hospital and Research Centre, Guntur.

Type of Study

Hospital based Cross sectional study

Period of study

One year study period

Method of Collection of Data

Data will be collected using a pretested proforma meeting the objectives of the study. Detailed history and necessary investigations will be undertaken. The purpose of the study will be explained to the patient and informed consent obtained. Minimum of 100 patients are selected randomly who will fulfil the inclusion and exclusion criteria. Relevant history including symptoms and signs at presentation, past medical history, menstrual history, drug history and examination findings will be noted.

Inclusion criteria

Postmenopausal women attending outpatient and inpatient of Medicine Department

Exclusion criteria

1. Known cases of diabetes mellitus, thyroid dysfunction, hypertension, chronic kidney disease.
2. Patients on Hormone replacement therapy
3. Diagnosed cases of ovarian and uterine malignancy
4. Patients on drugs like iodide, amiodarone, salicylates, propranolol, octreotide, phenytoin, lithium, glucocorticoid, amphetamine, aminoglutethemide, somatostatins.

Investigations

Routine Investigations

- Complete blood count
- Blood urea
- Serum creatinine
- Urine analysis
- FBS, PPBS
- ECG
- Chest X ray PA view
- USG abdomenopelvis

Special investigations

- Thyroid profile – TSH, Total T4.
- Lipid profile – Total cholesterol, Triglycerides, LDL cholesterol, HDL cholesterol.

Results

Study Design: A Clinical correlative study consisting of 100 patients, is undertaken to study the correlation of thyroid dysfunction with lipid levels in postmenopausal women.

Table 1: Age distribution of patients studied

Age in years	Number	%
45-49	7	7.0
50-54	31	31.0
55-59	33	33.0
60-64	29	29.0
Total	100	100.0

In our study, among 100 patients, 7 patients were in 45-49 years age group, 31 patients were in 50-54 years age group, 33 were in 55-59 years age group and 29 were in 60-64 years age group. Most were in 50-64 years age group. Mean age of patients in study was 56.5+/-5.47. Most patients were found to be in the 50 to 64 years of age group, with maximum in 55-59 years of age. Mean age of patients in study was 56.5+/- 5.47.

Table 2: Thyroid status of patients studied

Thyroid status	Number(n=100)	%
Euthyroid	68	68.0
Subclinical hypothyroid	22	22.0
Hypothyroid	8	8.0
Thyrotoxicosis	2	2.0

In our study, among 100 patients, 32 patients had thyroid dysfunction. Among these 32 patients, 22 patients were found to have subclinical hypothyroidism, 8 had clinical hypothyroidism and 2 had thyrotoxicosis. Remaining 68 were euthyroid. After screening 100 postmenopausal women, 22% had SH, 8% had overt hypothyroidism, 2% had thyrotoxicosis, remaining 68% were euthyroid.

Table 3: Correlation of Thyroid dysfunction of patients and age in years

Age in years	Total no. of patients	Thyroid dysfunction			
		Normal	SH	Hypo	Thyrotoxicosis
45-49	7	7(100%)	0(0%)	0(0%)	0(0%)
50-54	31	27(87.1%)	3(9.7%)	1(3.2%)	0(0%)
55-59	33	20(60.6%)	9(27.3%)	3(9.1%)	1(3%)
60-64	29	14(48.3%)	10(34.5%)	4(13.8%)	1(3.4%)
Total	100	68(68%)	22(22%)	8(8%)	2(2%)

In our study, in 45-49 years age group all 7 patients were euthyroid. In 50-54 years age group, among 31 patients, 3 patients had SH, 1 patient had hypothyroidism and remaining 27 patients were euthyroid. In 55-59 years age group, among 33 patients 9 patients had SH, 3 patients had hypothyroidism, 1 patient had thyrotoxicosis, remaining 20 patients were euthyroid. In 60-64 years age group, 10 patients had SH, 4 patients had hypothyroidism, 1 patient had thyrotoxicosis and remaining 14 patients were euthyroid.

Age in years was found to be significantly associated with thyroid dysfunction. With maximum SH patients in 55 to 64 years age group.

Table 4: Duration of menopause

Duration of menopause	Number (n=100)	%
0-4 years	23	24.0
5-9 years	40	40.0
10-14 years	34	33.0
15-19 years	3	3.0

In our study, among 100 patients, 23 patients had 0-4 years menopause duration, 40 patients had 5-9 years of menopause duration, 34 patients had 10-14 years menopause duration and 3 had 15-19 years menopause duration.

Among 100 patients, maximum had 5- 9 years of menopause duration.

Table 5: Correlation of Thyroid dysfunction of patients and Duration of menopause

Duration of menopause	Total no. of patients	Thyroid dysfunction			
		Normal	SH	Hypothyroid	Thyrotoxicosis
0-4 years	23	18(78.3%)	4(17.4%)	1(4.3%)	0(0%)
5-9 years	40	31(77.5%)	6(15.0%)	2(5%)	1(2.5%)
10-14 years	34	19(55.9%)	10(29.4%)	4(11.8%)	1(2.9%)
15-19 years	3	0(0%)	2(66.7%)	1(33.3%)	0(0%)
Total	100	68(68%)	22(22%)	8(8%)	2(2%)

In our study, among 23 patients with 0-4 years menopause duration, 4 patients had SH, 1 patient had hypothyroidism. Among 40 patients with 5-9 years menopause duration, 6 patients had SH, 2 patients had hypothyroidism, 1 patient had thyrotoxicosis. Among 34 patients with 10-14 years menopause duration, 10 patients had SH, 4 patients had hypothyroidism, 1 patient had thyrotoxicosis. Among 3 patients with 15-19 years menopause duration, 2 patients had SH and 1 patient had hypothyroidism.

Duration of menopause was found to be statistically associated with thyroid dysfunction.

Table 6: BMI distribution in the patients studied

BMI distribution	Number (n=100)	%
Up to 22.9	39	39.0
23 - 24.9 (overweight)	10	10.0
25.0 – 29.9 (grade 1 obesity)	34	34.0
> 30 (grade 2 obesity)	17	17.0

Maximum patients had a BMI of upto 22.9 i.e. 39% of patients had normal BMI. 10% of patients were overweight, 34 % were grade 1 obesity and 17 % of patients had grade 2 obesity. This BMI scale is according to the WHO classification of BMI in South Asian population. Healthy weight is BMI 18.5 – 22.9, Overweight is 23 – 24.9, Grade 1 Obese is 25 – 29.9. Grade 2 obesity is >30

Table 7: Correlation of Thyroid dysfunction of patients and BMI

BMI(kg/m2)	Total no. of patients	Thyroid dysfunction			
		Normal	SCH	Hypothyroid	Thyrotoxicosis
Up to 22.9	39	34(87.8%)	2(6.1%)	1(2.0%)	2(4.1%)
23 – 24.9	10	9(58.8%)	1(4.4%)	0(0%)	0(0%)
25.0 – 29.9	34	20(29.4%)	10(29.4%)	4(11.8%)	0(0%)
> 30	17	5(14.2%)	9(52.9%)	3(17.6%)	0(0%)
Total	100	68(68.0%)	22(22.0%)	8(8.0%)	2(2.0%)

In our study, among 39 patients with normal BMI, 2 patients had SH, 1 patient had hypothyroidism and 2 patients had thyrotoxicosis. Among 10 patients who were overweight (BMI 23-24.9) 1 patient had SH, rest were euthyroid. Among 34 patients with grade 1 obesity (BMI 25-29.9), 10 patients had SH, 4 patients had hypothyroidism. Among 17

patients with grade 2 BMI (BMI >30), 9 patients had SH and 3 patients had hypothyroidism. BMI was found to be significantly associated with thyroid dysfunction.

Table 8: Prevalence of dyslipidemia

Dyslipidemia	Number(n=100)	Percentage
Present	36	36%
Absent	64	64%

36% of the postmenopausal women had dyslipidemia. Remaining 64% did not have dyslipidemia.

Table 9: Correlation of Thyroid dysfunction of patients and Dyslipidemia

Dyslipidemia	Total no. Of patients	Thyroid dysfunction			
		Normal	SH	Hypo	Thyrotoxi -cosis
Absent	64	49(76.6%)	8(12.5%)	5(7.8%)	2(3.1%)
Present	36	19(52.8%)	14(38.9%)	3(8.3%)	0(0%)
Total	100	68(68%)	22(22%)	8(8%)	2(2%)

In our study, among 64 patients who did not have dyslipidemia, 8 patients had SH, 5 patients had hypothyroidism, 2 patients had thyrotoxicosis, rest were euthyroid.

Among 36 patients with dyslipidemia, 14 patients had SH, 3 patients had hypothyroidism and rest 19 were euthyroid.

Table 10: Correlation of thyroid dysfunction of patients and Pattern of Dyslipidemia

Pattern of Dyslipidemia	Total number of patients	Euthyroid	SH	Hypo	Thyrotoxic
Hypercholesterolemia	36	19 (52.77%)	14 (38.88%)	3 (8.33%)	0
Hypertriglyceridemia with hypercholesterolemia	5	0	4 (80.00%)	1 (20.00%)	0
Increased LDL with hypercholesterolemia	7	5 (71.42%)	0	2 (28.57%)	0
Low HDL with hypercholesterolemia	3	2 (66.66%)	0	1 (33.33%)	0

All patients with dyslipidemia, i.e 36 patients were found to have increased TC, of these 5 had increased TG, 7 had increased LDL, 3 had low HDL. In these 36 patients with dyslipidemia 19(52.77%) were euthyroid, 14(38.88%) were subclinically hypothyroid, 3(8.33%) were clinically hypothyroid. Dyslipidemia was not found in thyrotoxic patients. Predominant pattern of dyslipidemia seen in patients with thyroid dysfunction was hypercholesterolemia.

Table 11: Prevalence of IHD

IHD	Number n=100	%
Present	21	21%
Absent	69	69%

Among 100 patients, 21 patients were found to have ECG evidence of IHD.

Table 12: Pattern of ischaemic heart disease

ECG findings	Number (n=100)	%
Lateral wall ischaemia	2	2.0
Anteroseptal wall ischaemia	1	1.0
Old IHD	18	18.0
Normal	79	79.0

Among 21 patients with IHD, 2 had new lateral wall MI, 1 had anterior wall MI, 18 had evidence of old IHD.

Table 13: Correlation of Thyroid dysfunction of patients and ischaemic heart disease

Ischaemic heart disease	Total no. of patients	Thyroid dysfunction			
		Normal	SH	Hypo	Thyrotoxicosis
Absent	79	53(67.1%)	18(22.8%)	7(8.9%)	1(1.3%)
Present	21	15(71.4%)	4(19%)	1(4.8%)	1(4.8%)
Total	100	68(68%)	22(22%)	8(8%)	2(2%)

In our study, among 79 patients who did not have IHD, 18 patients had SH, 7 patients had hypothyroidism, 1 patient had thyrotoxicosis, rest 53 patients were euthyroid. Among 21 patients who had IHD, 4 patients had SH, 1 patient had hypothyroidism, 1 patient had thyrotoxicosis and 15 patients were euthyroid.

Discussion

Thyroid disorders are common endocrine disorders in adults. It is more common in females compared to males [1].

In females incidence increases with age. In females, many of the postmenopausal symptoms resemble symptoms of thyroid disorders. Hypothyroidism is associated with dyslipidemia which increases risk of CAD and other CVS disorders. Hyperthyroidism also associated with CVS disorders like arrhythmias. These thyroid disorders are potentially treatable conditions. The present study was intended to determine prevalence of thyroid disorder in postmenopausal women and their effect on lipid metabolism.

This study was conducted in the department of Medicine, NRI Medical College, Guntur, during a study period of 1 year. A total of 100 postmenopausal women attending the outpatient and inpatient in the department of medicine were included in the study and screened for thyroid dysfunction and lipid abnormalities.

In our study, most patients were found to be in 50 to 64 years age group with maximum in 55-59 years age group. Mean age of patients in study was 56.5 +_ 5.47 years. Out of 100 patients, 22 patients were found to have subclinical hypothyroidism, 8% had overt hypothyroidism and 2% had hyperthyroidism. According to Schindler A E the incidence of thyroid disease in postmenopausal women is as follows, clinical thyroid disease about 24%. Subclinical thyroid disease about 23.2%. Among the group of subclinical thyroid disease 73.8% are hypothyroid and 26.2% are hyperthyroid [12]. According to two studies the incidence of SH varies between 4 and 10% [9, 10].

Age was found to be significantly (P=0.052) associated with thyroid dysfunction with maximum patients of subclinical hypothyroidism in the 55 to 64 years of age. Pearce

E.N in his publication states that thyroid dysfunction is common among women over the age of 50. [2].

In our study, among 100 patients, maximum, that is 40 patients had 5-9 years of menopause duration. It was found that, with increasing duration of menopause the prevalence of hypothyroidism (both SH and clinical) also increased.

Maximum patients had a BMI of upto 22.9 i.e., 39% of patients had a normal BMI. 10% of patients were overweight and 34% were grade 1 obesity and 17% of patients had grade 2 obesity. BMI was significantly associated with thyroid dysfunction $P<0.001$. In our study, maximum patients had 5-9 years of menopause. Duration of menopause was found to be statistically associated with thyroid dysfunction (P=0.079).

In our study, 36% of patients had dyslipidemia. 38.9% of patients with subclinical hypothyroidism & 8.3% of clinical hypothyroid patients were found to have dyslipidemia. Presence of dyslipidemia was statistically associated with thyroid dysfunction with p = 0.014. Predominant pattern of dyslipidemia seen was hypercholesterolemia. EPIC – Norfolk prospective study found significantly increased concentration of serum total cholesterol (TC), LDL cholesterol (LDLc) and triglycerides in SH women. Similarly in a large cross sectional study an increase of 1.0 mIU/L in serum TSH was associated with an average rise in TC values of 0.09 mmol/L in women. In the latter study the impact of TSH elevation was substantially influenced by age, thus the effect of SH on the serum lipid profile appears more pronounced in women and is also worse with increasing age [11]. Meier *et al*. [12] reported a reduction of Serum TC by 0.29 mmol/L of LDLc by 0.33mmol/L after 12 months of L-thyroxine replacement. However the effect was most pronounced in patients with baseline serum TSH values >12mIU/L. similarly Caracio *et al*. [13] reported mean reductions in serum TC & LDLc concentrations of 0.47 & 0.41 mmol/L, respectively in a strictly selected group of patients with Hashimoto's thyroiditis & slightly elevated serum TSH level (<10mIU/L). In a subsequent randomised controlled study from the same group [14]. L-thyroxine replacement induced a significant improvement of both the lipoprotein profile and the carotid artery intima-media thickness: A widely recognised surrogate index of early atherosclerosis & CV events. A large metaanalysis in which individual data on more than 50,000 participants from 11 prospective cohorts were collected, demonstrated that CHD mortality was increased in participants with serum TSH >7 mIU/L & that the risk of CHD events was significantly increased once serum TSH >10mIU/L [15]. A recent observations analysis of 4500 SH patients from United Kingdom General Practitioner Research Database demonstrated that patients <70yrs who were started on L-thyroxine had lower CHD events over 8 years of follow up [16]. This suggests that L-thyroxine treatment of SCH is safe and the results are consistent with a modest prognostic benefit from such therapy.

In our study out of 100 patients, 21 patients were found to have IHD, remaining 79 patients did not have ECG evidence of IHD. Among these 21 patients with IHD, 1 had a new lateral wall MI, 1 had a new anterior wall MI and remaining 19 had evidence of old IHD in ECG. Among these 21 patients with IHD, 15 were euthyroid, 4 were subclinical hypothyroid, 1 was clinical hypothyroid and 1 was thyrotoxic. The presence of IHD was not statistically associated with thyroid dysfunction (p=0.697).

Conclusion

Thyroid dysfunction is seen in a significant percentage of postmenopausal women.

- In our study, the predominant dysfunction seen is subclinical hypothyroidism, followed by overt hypothyroidism. The incidence of thyrotoxicosis was very less in our study subjects.
- In our study, hypothyroidism, both SH and clinical hypothyroidism was seen more in women with increasing age.
- In our study, hypothyroidism, both SH and clinical hypothyroidism was seen more in women with increasing duration of menopause.
- In our study, hypothyroidism, both SH and clinical hypothyroidism was associated with increased BMI.
- In our study, dyslipidemia was significantly associated with thyroid dysfunction with predominant pattern being hypercholesterolemia.

In our study, presence of IHD in thyroid dysfunction patients was not statistically significant.

Postmenopausal women are at an increased risk for artherosclerosis and heart disease and the added presence of secondary dyslipidemia due to hypothyroidism in these women will add to the risk of atherosclerosis and its vascular complications. The presence of increased BMI as a consequence of undiagnosed hypothyroidism will further add to the risk factors for vascular complications.

Even subclinical hypothyroidism was associated with dyslipidemia and increased BMI. Hence screening can be recommended for hypothyroidism in postmenopausal women especially in those with increasing age, duration of menopause and overweight women to evaluate and correct dyslipidemia so as to prevent adverse artherosclerotic cardiovascular complications and to reduce morbidity and mortality. A larger study needs to be conducted in postmenopausal women to evaluate these factors.

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