



THYROID FUNCTION IN POSTMENOPAUSAL WOMEN IN WESTERN INDIA AND ITS IMPACT ON MENOPAUSAL SYMPTOMS, BMI, GLYCEMIC, LIPID AND CARDIAC PROFILE

General Medicine

Dr Dhvani Thakar Assistant Professor, Dept. of Medicine, Medical College Baroda

Dr Rupal Dosi Professor, Dept. of Medicine, Medical College Baroda

Dr Dnyaneshwar Maghade Senior Resident, Dept. of Medicine, Medical College Baroda

ABSTRACT

Background Menopause is characterized by estrogen deficiency and appearance of variety of menopausal symptoms like lethargy, hotflushes, anxiety, sexual problems, tiredness, insomnia, weight gain and mood swings. Many of these symptoms are similar to symptoms of thyroid dysfunction and hence there is likelihood of symptoms of thyroid dysfunction in this age group being misinterpreted as menopausal symptoms and thyroid dysfunction remaining undetected. If thyroid dysfunction remains undetected and untreated, it can lead to health hazards like hyperlipidemia, atherosclerosis and heart disease.² Presently there are no clear cut guidelines about screening menopausal patients for thyroid function and existing studies on screening of menopausal women for thyroid disorders are not conclusive. Therefore this study was undertaken to look at thyroid functions in postmenopausal women and impact of thyroid dysfunction on their cardiovascular health through its action on their glycemic status, BMI and lipid profile.

Aims And Objectives

1. To assess the basic thyroid functions in postmenopausal women.
2. To evaluate the effect of abnormal thyroid function on glycemic status, lipid profile, body weight and BMI in postmenopausal women.
3. To look for association of severity of menopause symptoms with the degree of thyroid dysfunction in postmenopausal women.

Materials And Methods

A cross-sectional observational study was carried out in the indoor and outdoor sections of Department of Medicine at SSG Hospital Vadodara for a period of one year from March 2015 to Feb 2016 in which 130 patients were enrolled. All patients were subjected to a standardized interview in which their symptoms were graded on the basis of the Simplified Menopausal Index, their BMI was calculated from their height and weight and investigations (Fasting thyroid profile, fasting blood sugar, fasting lipid profile, ECG) were carried out. Association between abnormalities in thyroid profile and severity of menopausal symptoms as well as abnormalities in BMI, fasting blood sugar, lipid profile and ECG were analyzed using appropriate statistical tests (Odd's ratio). A P value < 0.05 was considered statistically significant. **Conclusion** Thyroid dysfunction is common in postmenopausal females and the symptoms of the two entities overlap but with a higher intensity in the former and the simplified menopausal index score can be used as an efficient tool to further increase the index of suspicion for thyroid dysfunction in postmenopausal women. Abnormal thyroid function is statistically associated with BMI with higher prevalence of hypothyroidism in overweight, preobese and obese postmenopausal subjects and hyperthyroidism in underweight postmenopausal subjects. Abnormal thyroid function is statistically associated with abnormal glucose metabolism with higher prevalence of fasting hyperglycemia at either end of the spectrum of thyroid disorders. Abnormal thyroid function is statistically associated with Dyslipidemia in the form of raised total cholesterol, LDL cholesterol and serum triglycerides with no significant association with HDL cholesterol in postmenopausal women. There is no statistically significant association between thyroid dysfunction and ischemic heart disease.

KEYWORDS

Thyroid, Menopause symptoms, Diabetes, Lipid profile

INTRODUCTION

Menopause is a physiological process characterized by loss of reproductive function, depletion of ovarian follicles, state of estrogen deficiency and appearance of variety of menopausal symptoms like lethargy, hotflushes, anxiety, sexual problems, tiredness, insomnia, weight gain and mood swings. Many of these symptoms are similar to symptoms of thyroid dysfunction. It has also been observed that menopausal symptoms are more intense in patients with thyroid dysfunction.¹ There is likelihood of symptoms of thyroid dysfunction in this age group being misinterpreted as menopausal symptoms and thyroid dysfunction remaining undetected. If thyroid dysfunction remains undetected and untreated, it can lead to health hazard like hyperlipidemia, atherosclerosis and heart disease.² Even subclinical hypothyroidism can progress to overt hypothyroidism, especially if serum TSH (Thyroid stimulating hormone) concentration is >10 mIU/L.³ Further, there is evidence that subclinical hypothyroidism can be associated with elevated total and low density lipoprotein cholesterol levels and these levels improve with treatment with levothyroxine hormone.⁴ That is why timely detection of hypothyroidism is very important.

Metabolic syndrome, a cluster of factors like dysglycemia, dyslipidemia, central obesity and hypertension, is known to pronounce risk for future development of Type 2 diabetes mellitus and cardiovascular diseases.^[1] Studies show that Metabolic Syndrome and cardiovascular diseases are more common in women above 55 years of age with significant increase in individual risk factors in the postmenopausal phase.^{[2],[3]} Changing hormonal milieu with declining estrogen and alteration of its ratio with testosterone has been implicated as a causal factor for the emergence of Metabolic Syndrome

at menopausal transition.^{[4],[5]} Besides menopausal hormonal changes, ageing also contributes to clustering of cardio-metabolic risk factors at this time.^[6] Hence, there is a debate as to whether the increased incidence occurs due to ageing alone or due to menopausal transitional changes.

As women now spend one third to one half of their lives after menopause, screening can effectively detect the presence of subclinical thyroid dysfunction in postmenopausal women. Also, the assessment of thyroid function by modern assays is both reliable and inexpensive. Presently there are no clear cut guidelines about screening menopausal patients for thyroid function. Studies on screening of menopausal women for thyroid disorders are not conclusive. This study was carried out to look at thyroid functions in postmenopausal women.

MATERIALS AND METHODS

A cross-sectional observational study was conducted in the outdoor and indoor sections of Medicine department at SSG Hospital Vadodara from March 2015 to February 2016. By keeping 5% desired precision and expected prevalence of thyroid abnormality among postmenopausal women as 10% sample size comes to 129 patients ($\alpha=5\%$ I=95).

Inclusion Criteria:

Post menopausal women defined as those with more than 1 year of amenorrhea following last menstrual cycle.

Exclusion Criteria:

1. Patients on hormone replacement therapy

- Ovarian and uterine malignancy
- Patients on following drugs- Propranolol, Iopanoic acid, Iodide, Amiodarone, Salicylates, Phenytoin, Glucocorticoids, Lithium, Amphetamine, Sertraline, Aminoglutethimide, Interleukin, Dopamine, Somatostatin, Octreotide, Heroin use.
- Known case of cirrhosis of liver.
- Known case of nephrotic syndrome
- Renovascular hypertension.
- Known case of thyroid dysfunction from premenopausal state.

After taking written and informed consent about enrollment in the study and maintaining adequate privacy and confidentiality, all patients were subjected to a standardized interview. Symptoms of the patient were graded on the basis of the Simplified Menopausal Index. Complete medical and obstetric history was obtained and complete General and Systemic examination was done. Following investigations were carried out-

g) Investigations:

- Complete blood count (CBC)
- Urine routine
- Fasting Blood Sugar (FBS)
- Fasting basic thyroid profile
- S.TSH
- S.T3
- S.T4
- Fasting lipid profile
- S.Total Cholesterol
- S.Triglycerides
- S.LDL cholesterol
- S.HDL cholesterol
- ECG

h) Data Analysis:

All data was analyzed using appropriate statistical tests (Odd's ratio). A P value < 0.05 was considered statistically significant.

i) Outcome:

Evaluation of thyroid function in postmenopausal women attending outdoor and indoor sections of Medicine department, SSG Hospital, Vadodara and its association with

- Postmenopausal symptoms (using the Simplified Menopausal Index)
- Body weight (using Body mass index)
- Glycemic status (using Fasting blood glucose)
- Dyslipidemia (using lipid profile)
- Ischaemic heart disease (using ECG)

RESULTS

A total of 130 patients were enrolled in the study.

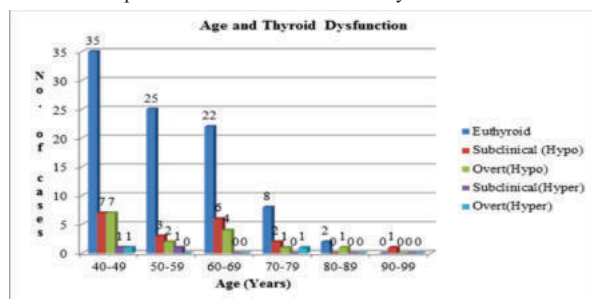


Figure 1

The age ranged from 40-90 years with mean of 54.7 ± 3.8 years. Majority [35, 26.9%] of the cases were in the age of 45-49 years, 16 [12.3%] cases were less than 45 years. 16 [12.3%] cases were above 70 years of age.

Thyroid dysfunction was seen in 26.8% cases of age < 50 years while it was seen in 33.3% of cases above 50 years. However the dysthyroid status was not significantly associated with any age group.

Out of total 130 cases, most had menopause in last 4 years [44, 33.8%] and 26 [20%] had menopause in last 5-9 years, remaining 60 [46.2%] women had it since more than 10 years. Thyroid dysfunction was seen in 25% of cases whose duration of menopause was < 19 years, while it

was seen in 36% of cases with duration of menopause > 19 years, but this difference was statistically not significant.

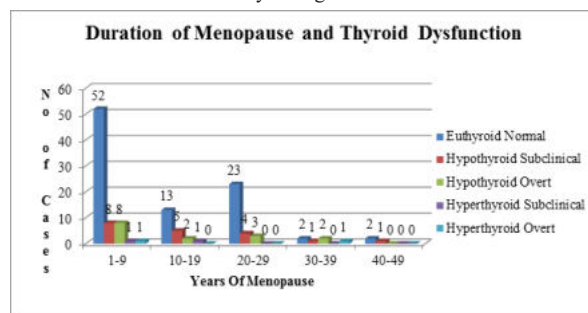


Figure 2

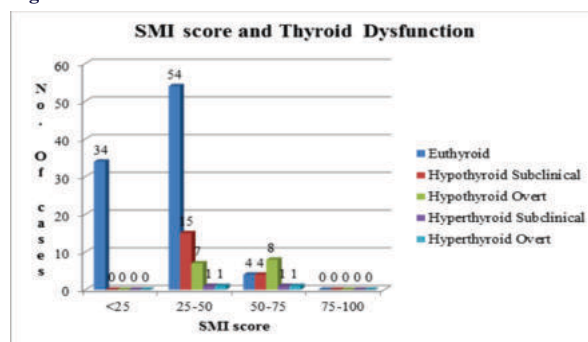


Figure 3

It was seen that 30.7% of patients with SMI score of 25-50 and 77.7% of patients with SMI score of 50-75 had thyroid dysfunction. This finding was statistically highly significant ($p < 0.001$).

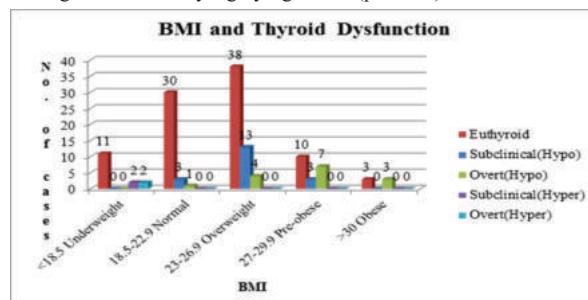


Figure 4

Majority of patients (42.3%) were overweight followed by normal weight (26.15%) while 11.53% were underweight, 15.38% were pre-obese and 4.61% were found to be obese.

Hyperthyroidism was observed in 26.6% cases whose BMI was < 18.5 while hypothyroidism was seen in 37% of cases with BMI > 23. This was statistically significant [$p = 0.02$]

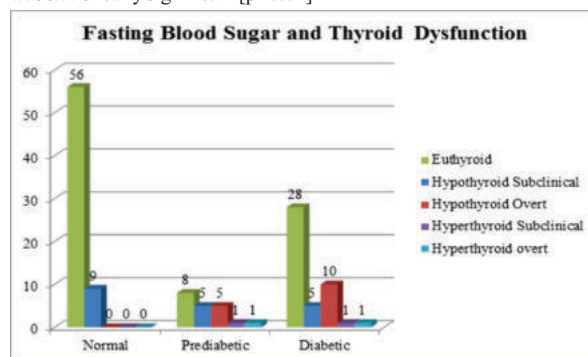


Figure 5

Among our 130 cases Diabetes was diagnosed in 45 [34.6%] cases and 20 [15.4%] cases were pre diabetics while remaining 65 [50%] cases were non diabetics.

Dysthyroidism was observed in 16% of the non diabetics while it was

found in 37.7% cases who were diabetics, this was statistically highly significant [$p=0.009$]

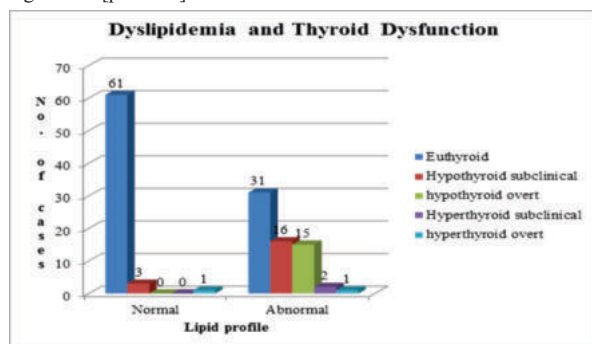


Figure 6

Out of 130 cases dyslipidemia was found in 67 [51.5%] cases and remaining 63 [48.5%] cases had normal lipid profiles.

Out of 65 cases with dyslipidemia, 34 [51%] had abnormal thyroid function while out of 65 cases of normal lipid levels, only 4 had abnormal thyroid function. This was statistically highly significant. [$p<0.001$]

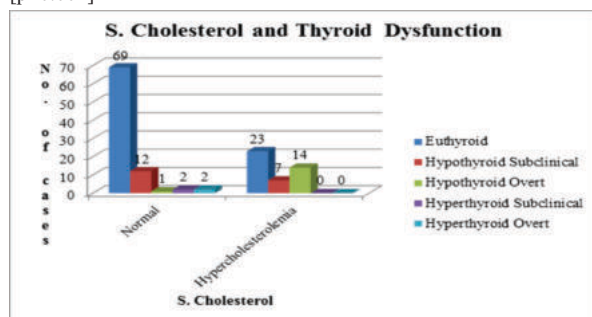


Figure 7

The serum cholesterol level was high in 44 cases and it was normal in 86 cases. Among cases with hypercholesterolemia abnormal thyroid level was seen in 21 [47.6 %] cases while it was seen only in 28.5 % cases with normal cholesterol. This difference was statistically significant [$p=0.029$].

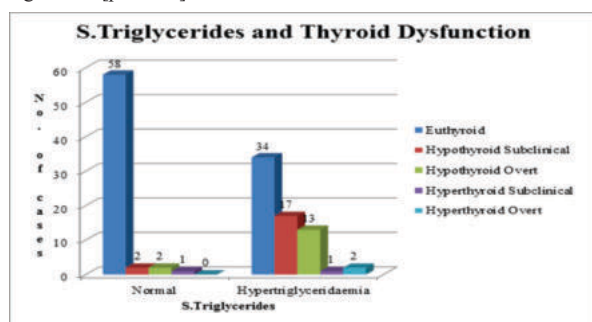


Figure 8

High TG level was seen in 67 cases and normal in 63 cases. Thyroid dysfunction was observed in 35 [49%] cases with hyper triglyceridemia, while it was only in 3 [8%] cases with normal serum triglyceride level. This difference was statistically significant. [$p<0.001$]

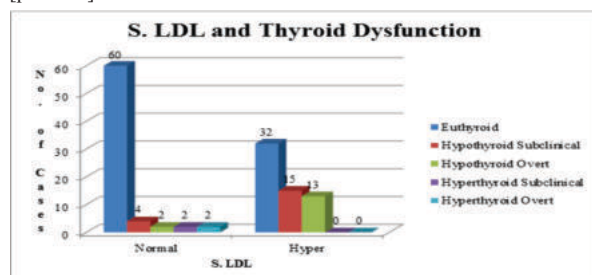


Figure 9

High LDL level was seen in 60 cases and normal in 70 cases. Thyroid dysfunction was observed in 28 [46.7%] cases with high LDL, while it was only in 10 [14 %] cases with normal LDL level. This difference was statistically significant. [$p<0.001$]

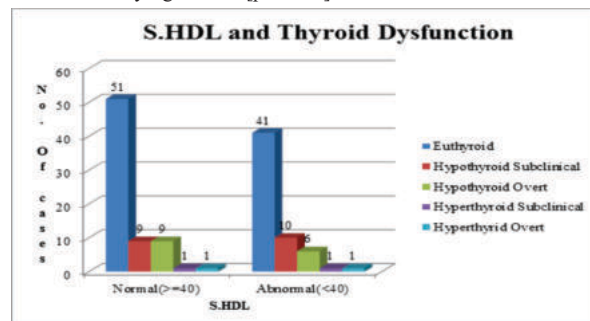


Figure 10

Low HDL level was seen in 71 cases and normal in 59 cases. Dysthyroidism was observed in 20 [28%] cases with Low HDL, and it was in 28 [30.5%] cases with normal HDL level. There was no significant difference found statistically. [$p=0.77$]

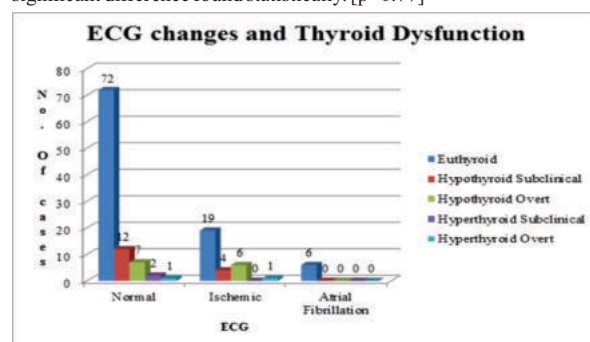


Figure 11

Out of 130 cases of our study, 30 [23%] cases had Ischemia in their ECG and 6 [4.6 %] had Atrial fibrillation.

11 [36.6%] of the cases with ischemia had abnormal thyroid function while 22 [23. 4%] cases with normal ECG had thyroid dysfunction. This finding was statistically insignificant. [$p=0.056$].

DISCUSSION

Prevalence of thyroid dysfunction in the postmenopausal subjects was found to be 29.1% in our study, the distribution of which is as follows:

- Hypothyroidism 26.1%
- Subclinical hypothyroidism 16.9%
- Overt hypothyroidism 9.2%
- Hyperthyroidism 3%
- Subclinical hyperthyroidism 1.5%
- Overt hyperthyroidism 1.5%

This result is comparable to following published studies

- Joshi S. A. et al, Nagpur, Maharashtra-Out of 200 women 25 women had raised TSH levels. Three women had overt hypothyroidism (TSH high, free T4 low), and 22 women had subclinical hypothyroidism (TSH high, free T4 normal).
- Schindler et al., IMRE, Essen Germany-the prevalence of clinical thyroid disease in postmenopausal women was about 2.4%; subclinical thyroid disease, about 23.2%. Among the group with subclinical thyroid disease, 73.8% are hypothyroid and 26.2% are hyperthyroid.
- Suchartwatnachai C et al., in a post menopause clinic in Bangkok, Thailand the prevalence of hypothyroidism was 25%

A majority of patients (24.61%) included in this study fell in the age group of 45-49 years with mean age of patient 54.7 ± 3.8 years.

Abnormal thyroid function was seen in 26.8 % cases of age <50 years while it was seen in 33.3 % of cases above 50 years with percentage of euthyroid subjects falling with increasing age and percentage of dysthyroid subjects rising with increasing age. However the dysthyroid status was not significantly associated with any age group. [$p=0.64$].

This is in accordance to the study by Elizabeth N Pearce, Boston University Medical Center, Boston, Massachusetts, USA in which thyroid dysfunction was common, especially among women over the age of 50 years.

The serum level of Thyroid Binding Globulin increases with age, while serum levels of circulating thyroid hormones decrease¹⁰⁸ which is probably related to aging of the thyroid gland and atrophic thyroiditis.

Out of total 130 cases, most had menopause in last 4 years [44, 33.8%] and 26 [20%] had menopause in last 5-9 years, while the remaining 60 [46.2%] had menopause for more than 10 years.

Thyroid dysfunction increased progressively with duration of menopause with abnormal thyroid function tests in 25 % of cases whose duration of menopause was <19 years, while the same was in 36 % of cases with duration of menopause >19 years, but this difference was statistically not significant. [$p=0.17$]. This finding occurs secondary to increasing age of the patient with increasing years of menopause.

The symptoms of the patients were graded according to the simplified menopausal index and prevalence of thyroid dysfunction was compared between mild (0-25), moderate (25-50) and high (75-100) scores. It was seen that 30.7% of patients with SMI score of 25-50 and 77.7% of patients with SMI score of 50-75 had thyroid dysfunction. This finding was statistically significant ($p<0.001$).

This result is similar to study conducted by

1. Joshi S. A. et al, NKP Salve Institute of Medical Sciences, Nagpur, Maharashtra, India
2. R Marahatta (Khanal) Department of OBGYN, Nepal Medical College Teaching Hospital, Kathmandu, Nepal
3. Badawy et al., Mansoura University Hospitals, Mansoura, Egypt
4. Oi N. et al, Tokyo Women's Medical University East Medical Center.

These studies showed that marked improvement in the menopausal-like symptoms occurred after treatment of the thyroid dysfunction. Elderly women with severe or resistant menopausal symptoms can be offered TSH, T3 and T4 assays to rule out the thyroid disturbances before attempting hormone replacement therapy.

In our study ,majority of patients(55,42.3%) were overweight followed by normal weight(34,26.15%) while 15 (11.53%) were underweight, 20 (15.38%) were pre-obese and 6 patients(4.61%) were found to be obese.

Among these hyperthyroidism was observed in 26.6% cases whose BMI was <18.5 while hypothyroidism was seen in 37% of cases with BMI >23. This was statistically significant [$p=0.02$]

Similar results have been reported by

1. Pandey S. et al, Medical Research Centre of Kasturba Health Society, Mumbai- Prevalence of MS amongst postmenopausal women was significantly higher ($P < 0.001$) than that in premenopausal women by both, IDF (premenopausal 45% and postmenopausal 55%) and H₁ MS criteria
2. Tehrani F.R. et al, Shahid Beheshti University of Medical Sciences, Tehran, Iran-The prevalence of obesity/overweight in women with SCH was higher than that in euthyroid women.
3. Michalaki M. et al, University Hospital, Patras, Greece.-Thyroid parameters in 144 morbidly obese patients. The prevalence of hypothyroidism. Eleven percent (11.8%) carried the diagnosis of hypothyroidism and were undergoing levothyroxine (LT₄) replacement therapy, 7.7% had newly diagnosed subclinical hypothyroidism, 0.7% had subclinical hyperthyroidism and 7.7% were euthyroid.

Among our 130 cases Diabetes was diagnosed in 45 [34.6%] cases and 20 [15.4%] cases were prediabetics while remaining 65 [50%] cases were non diabetics. Thyroid dysfunction was observed in 16% of the non diabetics while it was found in 37.7% cases who were diabetics, this was statistically highly significant [$p=0.009$].

This finding is in concordance with Marina A. Michalaki et al, University Hospital, Patras, Greece in which serum TSH concentration was associated with fasting serum insulin levels and

insulin resistance but not with serum leptin levels, body mass index (BMI), fat mass, and lean body mass. These subjects had higher levels of T₃, FT₃, T₄, and TSH, probably the result of the reset of their central thyrostat at higher level.

Out of 130 cases dyslipidemia was found in 67 [51.5%] cases and remaining 63 [48.5%] cases had normal lipid profiles. Out of 67 cases with dyslipidemia, 34 [51%] had abnormal thyroid function while out of 63 cases of normal lipid levels, only 4 had abnormal thyroid function. This was statistically highly significant. [$p<0.001$]

The serum cholesterol level was high in 44 cases and it was normal in 86 cases. Among cases with hypercholesterolemia abnormal thyroid level was seen in 21 [47.6 %] cases while it was seen only in 28.5 % cases with normal cholesterol. This difference was statistically significant [$p=0.029$].

High TG level was seen in 67 cases and normal in 63 cases. Abnormal thyroid function was observed in 35 [49%] cases with high serum triglycerides, while it was only in 3 [8%] cases with normal triglyceride level. This difference was statistically significant. [$p<0.001$]

High LDL level was seen in 60 cases and normal in 70 cases. Thyroid dysfunction was observed in 28 [46.7%] cases with high LDL, while it was only in 10 [14 %] cases with normal LDL level. This difference was statistically significant. [$p<0.001$]

Low HDL level was seen in 71 cases and normal in 59 cases. Thyroid dysfunction was observed in 20 [28%] cases with Low HDL, and it was in 28 [30.5%] cases with normal HDL level. There was no significant difference found statistically. [$p=0.77$]

- Marwaha R. K. et al, Institute of Nuclear Medicine & Allied Sciences, Delhi, India-Serum total cholesterol (TC), and LDL cholesterol (LDL) were significantly higher in adults with TSH > 10 mIU/L compared to controls. There were no significant changes in lipid parameters in subjects with SCH having TSH $\leq$ 10.0 mIU/L, compared to controls. Serum TSH was positively and FT3 and FT4 were negatively correlated with TC and LDL.
- Tehrani F. R. et al, Shahid Beheshti University of Medical Sciences, Tehran-After adjustment for BMI there were no statistically significant associations between TSH and total cholesterol, LDL or FBS, but there was a significant negative association between TSH and HDL ($p=0.001$, $r=-0.115$)
- Duntas L. H. et al, University of Athens Medical School, Athens, Greece.-Hyperthyroidism exhibits an enhanced excretion of cholesterol and an increased turnover of LDL resulting in a decrease of total and LDL cholesterol, whereas HDL are decreased or not affected. Subclinical hypothyroidism (SH) is associated with lipid disorders that are characterized by normal or slightly elevated total cholesterol levels, increased LDL, and lower HDL.

The composition and the transport of lipoproteins are seriously disturbed in thyroid diseases. Overt hypothyroidism is characterized by hypercholesterolaemia and a marked increase in low-density lipoproteins (LDL) and apolipoprotein B (apo B) because of a decreased fractional clearance of LDL by a reduced number of LDL receptors in the liver. The high-density lipoprotein (HDL) levels are normal or even elevated in severe hypothyroidism because of decreased activity of cholesteryl-ester transfer protein (CETP) and hepatic lipase (HL), which are enzymes regulated by thyroid hormones.

Out of 130 cases of our study, 30 [23%] cases had Ischemia in their ECG and 6 [4.6 %] had Atrial fibrillation. 11 [36.6%] of the cases with ischemia had abnormal thyroid function while 22 [23. 4%] cases with normal ECG had thyroid dysfunction. This finding was statistically insignificant. [$p=0.056$].

Subclinical hypothyroidism has been associated with endothelium dysfunction, aortic atherosclerosis, and myocardial infarction. Lipid disorders exhibit great individual variability. Nevertheless, there might be a link, although it has not been proved, between thyroid dysfunction and atherosclerosis.

CONCLUSION

From this study we conclude that Thyroid dysfunction is common in postmenopausal females and the symptoms of the two entities overlap but with a higher intensity in the former and the simplified menopausal index score can be used as an efficient tool to further increase the index of suspicion for thyroid dysfunction in postmenopausal women.

Abnormal thyroid function is statistically associated with BMI with higher prevalence of hypothyroidism in overweight, preobese and obese postmenopausal subjects and hyperthyroidism in underweight postmenopausal subjects.

Abnormal thyroid function is statistically associated with abnormal glucose metabolism with higher prevalence of fasting hyperglycemia at either end of the spectrum of thyroid disorders.

Abnormal thyroid function is statistically associated with Dyslipidemia in the form of raised total cholesterol, LDL cholesterol and serum triglycerides with no significant association with HDL cholesterol in postmenopausal women.

There is no statistically significant association between thyroid dysfunction and ischemic heart disease.

REFERENCES

1. Elizabeth N Pearce Thyroid dysfunction in perimenopausal and postmenopausal women *Post Reprod Health March 1, 2007* vol. 13 no. 1 8-13
2. E. Schindler Thyroid function and Postmenopause *Journal of Gynaecological Endocrinology* 2003, Vol. 17, No. 1, Pages 79-85
3. Oi N, Ohi K Comparison of the symptoms of menopause and symptoms of thyroid disease in Japanese women aged 35-59 years. *Climacteric*. 2013 Oct;16(5):555-60.
4. Suchartwatnachai C; Theppaisai U; Jirapinyo M Screening for hypothyroidism at a menopause clinic. *International Journal of Gynecology and Obstetrics*. 2002; 77:39-40.
5. A.Badawy, O. State, and S. Sherief Can thyroid dysfunction explicate severe menopausal symptoms? *Journal of Obstetrics & Gynaecology* 2007, Vol. 27, No. 5 , Pages 503-505
6. Pandey S, Srinivas M, Agashe S, Joshi J, Galvankar P, Prakasam C P, Vaidya R. Menopause and metabolic syndrome: A study of 498 urban women from western India. *J Mid-life Health* 2010;1:63
7. Marina A. Michalaki, Apostolos G. Vagenakis, Aggeliki S. Leonardou, Marianna N. Argentou, Ioannis G. Habeos, Maria G. Makri, Agathoklis I. Psyrogiannis, Fotis E. Kalfarentzos, and Venetsana E. Kyriazopoulou. 2006 Thyroid function in humans with morbid obesity. *Thyroid*. February 2006, 16(1): 73-78.
8. Duntas LH, 2002 Thyroid disease and lipids. *Thyroid* 12: 287-293.
9. Tehrani FR, Tohidi M, Dovom MR, Azizi F (2011) A Population Based Study on the Association of Thyroid Status with Components of the Metabolic Syndrome. *J Diabetes Metab* 2:156.
10. Hak AE, Pols HAP, Visser TJ, Drexhage HA, Hoffman A, Witteman JCM, 2000 Subclinical hypothyroidism is an independent risk factor for atherosclerosis and myocardial infarction in elderly women: the Rotterdam Study. *Ann Intern Med* 132: 270-278.
11. Samuels MH, 1998 Subclinical thyroid disease in the elderly. *Thyroid* 9: 803- 813.
12. Luboshitzky R, Aviv A, Herer P, Lavie L, 2002 Risk factors for cardiovascular disease in women with subclinical hypothyroidism. *Thyroid* 12: 421-425.
13. Aviram M, Luboshitzky R, Brook JG, 1982 Lipid and lipoprotein pattern in thyroid dysfunction and the effect of therapy. *Clin Biochem* 15: 62-66.
14. Cooppan R, Kozak GP, Hyperthyroidism and diabetes mellitus, *Arch Intern Med* 1980; 140: 372-373.
15. Samantray SK, Pulimood BM, Koshy TS. Coexistence of diabetes and hypothyroidism in South Indian. *Med J. Act* 1977; 15; 60-62.
16. Harrison's Principles of Internal Medicine; 19th edition; Vol 2: 2233-2235.
17. Ladenson PW, Singer PA, Ain KB, Bagachi N, Bigas ST, Levy EG, et al. American Thyroid Association guidelines for detection of thyroid dysfunction. *Archives of Internal Medicine*. 2000; 160: 1573-5.
18. Suchartwatnachai C; Theppaisai U; Jirapinyo M Screening for hypothyroidism at a menopause clinic. *International Journal of Gynecology and Obstetrics*. 2002; 77:39-40.