

A Study of Thyroid Profile in Perimenopausal Women to rule out Subclinical Hypothyroidism and its relation to Cholesterol Levels

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Abstract:

Introduction: Subclinical hypothyroidism (SCH) is common in elderly women. It is associated with serious complications. Substantial number of patients have risk of SCH getting converted into primary hypothyroidism.

Aim of the study: The objectives of present study is to find out the prevalence of SCH in perimenopausal women and its relation to cholesterol levels in patients attending the medicine and gynaecology outpatient department of SMIMS.

Materials and Methods: A cross sectional study was conducted with sample size comprising of 60 patients who were attending the OPD of medicine and gynaecology in SMIMS. Assessment of thyroid function in serum of all the patients and assessment of serum cholesterol in patients diagnosed to be SCH was performed by ELISA method over a period of one year.

Results&Discussion: Total number of patients were 60. All were females in the age group 40 to 55 years. Subjects having elevated serum TSH with normal fT3 and fT4 were considered as SCH. 10 patients had SCH, 1 patient had overt hypothyroidism and the remaining 49 were euthyroid. In the patients who were diagnosed to have SCH, 70% of the individuals had hypercholesterolemia.

Conclusion: The percentage of SCH amongst the study sample patients was 17%, which is quiet high in the perimenopausal period. Their cholesterol levels were also raised in 70% of the patients with SCH. On the basis of the present study we suggest that routine screening of perimenopausal women with or without symptoms is mandatory. Timely detection and proper management of these problems will help in reducing the morbidity and preventing further complications.

Keywords: Subclinical Hypothyroidism, Thyroid dysfunction, Hyperlipidemia, Perimenopause, Autoimmune.

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I. Introduction

In India, among the endocrine diseases thyroid disorder is considered to be the most common. About 42 million people are being affected by thyroid disorder throughout India. [1] The prevalence of this disorder varies according to the age, sex, race, geographical factors and presence of antithyroid antibodies. [2,3] The elevated levels of thyroid stimulating hormone (TSH) with normal levels of free triiodothyronine (fT3) and free thyroxine (fT4) is known as subclinical hypothyroidism. [4] Most of the patients are asymptomatic, however some may have mild nonspecific symptoms of hypothyroidism like weight gain, loss of hair, constipation, menstrual irregularities etc. Evidences suggest that persons with SCH have increased cardiovascular mortality. [5] Subclinical hypothyroidism is more common in elderly women. [6] The overall prevalence of this disorder in elderly women is 17%. [7] Based on the most recent data subclinical hypothyroidism is approximately 14 times more common than overt hypothyroidism. [8] In United states 0.3% have overt hypothyroidism and 4.3% have subclinical hypothyroidism. [9] SCH is usually so insidious that the typical manifestations may take months or years to appear and go unnoticed by family and friends. Although most of the individuals progress slowly to overt hypothyroidism with cardiovascular, renal or neurological complications, rapid progression over weeks to months have been reported. [10] One of the predisposing factor for rapid progression is advancing age. Women suffering from SCH had progressed to overt hypothyroidism at the rate of 3-18% per year. [11]

SCH patients have shown increased cholesterol levels. [12] The increased association of subclinical hypothyroidism with aortic atherosclerosis and myocardial infarction has been recently reported from Rotterdam study. Reports have suggested that for every elevation in serum thyroid stimulating hormone of one microgram per millilitre there is an elevation in cholesterol level of about 0.09 millimoles per L which is about three to five milligrams per decilitre among women. [13] Perimenopausal period is the period around menopause. It extends from 40 to 55 years. It is the period during which a woman passes from the reproductive to the non-reproductive stage. [14] The high prevalence of SCH and difficulty in making the diagnosis in older patient's due to non-

specific symptoms like mild lassitude, cold intolerance, constipation and menstrual irregularities which mimics the menopausal symptoms, screening for SCH may be useful in perimenopausal women. Even though there are studies which prove SCH is associated with increased cholesterol levels, some studies do not agree with this statement. So, the present study was done to find out the association of SCH with cholesterol levels and also to determine the incidence of subclinical hypothyroidism in perimenopausal women.

II. Materials and Methods

After getting approval from the institutional ethical committee this cross-sectional study was done. This study was conducted at SreeMookambika institute of medical sciences, kulasekharam in a time period of one year. 60 persons were selected non-randomly of the age group 40 to 55 years from the Outpatient Department of General Medicine and Gynaecology, SreeMookambika Institute of Medical Sciences Hospital, Kulasekharam after considering the Inclusion and Exclusion criteria. After keeping the patient in a comfortable position and in fasting condition, 5ml of venous blood is collected from the median cubital vein in a plain sterile test tube. No anticoagulants or additives added to it. The sample is left without disturbing to clot. The serum is then separated by centrifugation. Estimation of T3, T4 and TSH was done by ELISA method [15], and the estimation of cholesterol by cholesterol oxidase – peroxidase method [16].

III. Figures And Tables

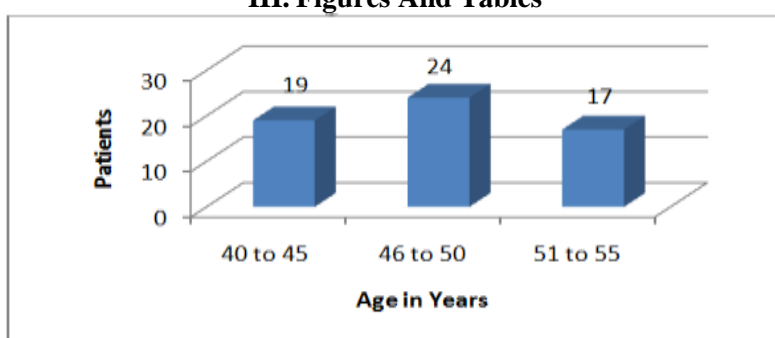


Fig 1- Age distribution

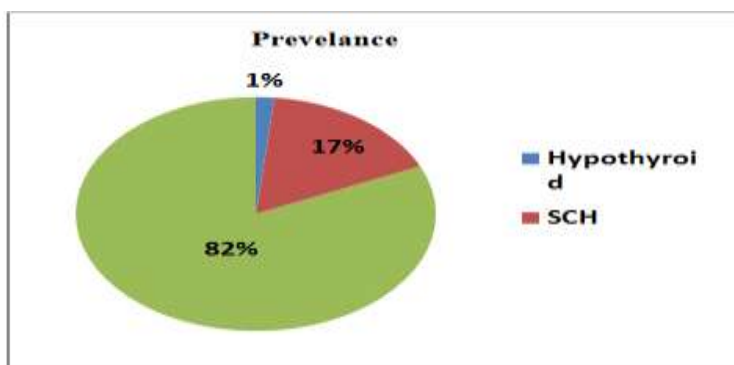


Fig 2- Prevalance of subclinical hypothyroidism in perimenopausal women (40 to 55 years)

Parameters	Patients	Minimum	Maximum	Mean	Std. Deviation (±)
Age (yrs)	60	40	55	48.3	4.05
Pulse/min	60	60	88	75.5	5.60
Systolic BP (mm of Hg)	60	90	130	117.16	7.15
Diastolic BP (mm of Hg)	60	70	80	76.93	4.61
Weight(kg)	60	40	73	56.28	7.47
Height(cm)	60	140	167	154.03	6.11
BMI(wt in kg/ht in m ²)	60	16.46	32.65	23.84	3.32
FreeT3(serum)	60	1.01	6.13	3.74	1.00
FreeT4(serum)	60	3.54	22.74	15.26	3.36
TSH(serum)	60	1	32.24	4.86	5.98

Table 1 - Baseline characteristics of the study group

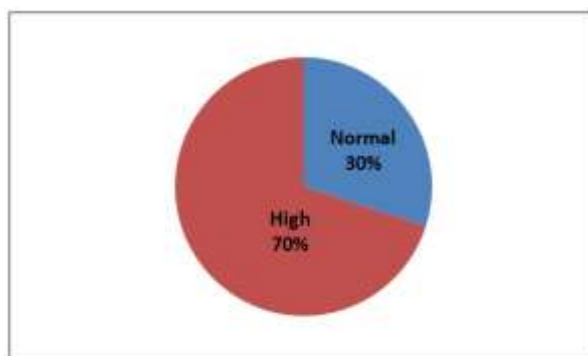


Fig 3 - Association of subclinical hypothyroidism with cholesterol levels

IV. Results

In our study prevalence of SCH in perimenopausal women (40 to 55years) was 17% (10 patients affected out of 60 persons under study). In these patients who have been diagnosed to have SCH, 70% of the individuals had hypercholesterolemia and it has a statistically significant correlation with SCH. There were 60 persons taken for this study. Out of them, 19 persons come under the category of 40 to 45 years, 24 persons come under the category of 46 to 50 years and the remaining 17 persons come under the category of 51 to 55 years. The minimum age of the person participated in the study is 40 years and maximum age of the participant is 55 years (fig-1).

According to the parameters, the minimum pulse rate is 60/min and maximum is 88/min with the mean and standard deviation of 75.5 and 5.60. Minimum systolic BP is 90mm of Hg and maximum is 130 mm of Hg with the mean and standard deviation of 117.16 and 7.15 followed by diastolic BP minimum 70 mm of Hg and maximum 80mm of Hg with mean and standard deviation of 76.93 and 4.61. Minimum weight is 40kg and maximum is 73kg with mean and standard deviation of 56.28 and 7.47. Minimum height is 140cm and maximum is 167cm with mean and standard deviation of 154.03 and 6.11. Minimum BMI is 16.46 and maximum is 32.65 with mean and standard deviation of 23.84 and 3.32.

Minimum serum free T3 level is 1.01pmols/L and maximum is 6.13pmols/L with mean and standard deviation of 3.74 and 1.00. Minimum serum free T4 level is 3.54pmols/L and maximum is 22.74pmols/L with mean and standard deviation of 15.26 and 3.36. Minimum serum TSH level is 1mIU/L and maximum is 32.24mIU/L with mean and standard deviation of 4.86 and 5.98 respectively (Table-1).

In our study, out of 60 persons, 10 persons (17%) were affected by subclinical hypothyroidism, 1 person (1%) was affected by overt hypothyroidism and the remaining 49 persons (82%) were normal represented by pie diagram (Fig 2). Out of 10 patients diagnosed to have subclinical hypothyroidism, 7 patients (70%) had increased serum total cholesterol level and the remaining 3 patients (30%) had normal serum total cholesterol level represented by pie diagram (Fig 3).

V. Discussion

The earliest form of hypothyroidism is called subclinical hypothyroidism which is also called as mild thyroid failure, reduced thyroid reserve, or preclinical hypothyroidism. [17] SCH is a type of thyroid dysfunction where the thyroid stimulating hormone level in serum is increased with a normal serum freeT3 and freeT4 levels. [4] In SCH the clinical as well as biochemical changes varies from individual to individual. Some may have mild symptoms while others may be severely affected. Even though SCH is solely dependent on the biochemical profile there are some individuals who present with signs and symptoms of hypothyroidism. [9] It has been estimated that about 20 million people in European union and over 14 million in United states are affected by SCH. The number of patients with SCH has increased worldwide due to widespread availability of TSH measurement. [7]

Different studies utilize different TSH cut off values for diagnosing SCH. According to Nystrom et al studies the reference TSH cut off value is above 8mIU/L. [18] In our study the maximum upper level of serum TSH concentration of 6.16mIU/L was considered to be normal and for serum freeT3 and free T4 6.45pmols/L and 25.80 pmols/L respectively. So, any increase in the serum TSH values above 6.16mIU/L and with serum FT3 and FT4 within normal limits were considered to be diagnosed as a case of SCH. Because SCH is uncommon in younger age group and the incidence is low in males and also in younger age group there is no well-defined therapy for abnormalities in cholesterol, our study has been focused to perimenopausal women between the age group of 40 to 55 years. Our study has shown that SCH was the most prevalent thyroid disorder followed by overt hypothyroidism in perimenopausal women. The prevalence of SCH varies depending on the age, sex, ethnicity, race, socioeconomic status and dietary habits of the population under study. Our study has shown a prevalence of 17% among the perimenopausal women. The prevalence is quiet high in our study and it

correlates with some studies. In one study, the prevalence was reported to be 23.9% in a population where people consume surplus amount of iodine and the incidence was 4.2% in a population where iodine consumption is less. [19]

The study conducted among male and female of the ethnic population of mountainous valley of Kashmir concluded with a total highest prevalence of SCH to be 21.56% and the prevalence was more in females about 81.8%.¹ In two more studies the prevalence of SCH was about 3-8% and 4-15% respectively and it increases with age and also common in women. As many studies states, the increased prevalence of SCH in our study in this age group may be due to iodine excess and the presence of anti TPO antibodies and not due to iodine deficiency because iodine status improvement has occurred during the last 2 to 3 decades of salt iodization. However, the iodine status as well as anti TPO antibodies were not evaluated in these females in our study. The differences in prevalence may be due to difference in the study areas and the different upper normal limit of serum TSH. A study by Tanis et al about SCH and its association with cholesterol levels indicated an elevated cholesterol level with increase in serum TSH levels (ie) an increase of 5mIU/L higher than the normal of TSH lead to an increase in 0.5mmol of total cholesterol. [20] Several studies report that SCH is associated with hypercholesterolemia. [21] Moradi et al found increased cholesterol levels in SCH patients. [22] A series of studies reported that the increase in the level of TSH is strongly associated with lipid abnormalities. There are several other studies which does not accept the association of increased TSH with increased cholesterol. A study was conducted by the Austrian to compare the cholesterol levels between SCH and normal individuals. The study group consists of 1055 persons with SCH and 4856 persons with normal thyroid function, on evaluation both these groups didn't show much changes in their cholesterol levels. [23] Moreover the association between SCH and dyslipidemia is still a matter of doubt.

Recently it has become popular to find the association between elevated TSH and elevated TC and is under research. It is Interesting to note that majority of the research is carried out to find the relation between serum TSH and lipid profile in euthyroid individuals. Many other studies have previously ruled out a positive correlation that whenever there is increased serum TSH concentration the lipid parameters also increase. Similarly, our analysis also shows a significant positive correlation with increased TSH and its associated elevated cholesterol levels. This was also statistically significant according to their p-value 0.01. The in vitro and in vivo research done by a laboratory, studied about the TSH functions and reported that serum TSH irrespective of fT3 and fT4 can independently up regulate the expression of the rate limiting enzyme of cholesterol synthesis (HMG CoA reductase). [24] Thus it is hypothesized that elevation in serum TSH alone as seen in SCH would be positively associated with hypercholesterolemia. The other parameters in our study like the age, height, systolic BP, diastolic BP didn't correlate significantly with abnormal TSH except the pulse rate which showed bradycardia with increase in serum TSH. It is statistically significant according to their p-value <0.05. The BMI correlates with increased TSH but it is not statistically significant. The positive correlation is similar to some studies which shows a positive association between TSH and BMI. Individuals with increased TSH values were associated with increased BMI. This association between TSH and body weight is caused by signals from adipose tissues. [25] Mainenti MR et al conducted a study among adult women between the age 30 to 60 years found bradycardia in patients with SCH. There are studies which shows the relation between TSH and age.

In order to justify whether screening for thyroid dysfunction is necessary in the perimenopausal age group, we determined the prevalence of SCH in this age group between 40 -55years. Even though the association between subclinical hypothyroidism, hypercholesterolemia and coronary artery disease is still a matter of confusion, there are many studies which confirm the close relationship between these three. A recent meta-analysis and a cross sectional Rotterdam study showed the risk of dyslipidemia and coronary artery disease in SCH. [13] So, we estimated the serum total cholesterol levels, so that earlier the diagnosis and treatment may prevent the patient from going into complications, since increased TC is the risk factor for atherosclerosis and myocardial infarction. The treatment of SCH is again a question of debate, but many studies have proved beneficial effects to the patients by decreasing the signs and symptoms and also by preventing the progression to overt hypothyroidism. [26] Though screening for hypothyroidism is cost effective many studies have recommended screening because some persons with SCH may or may not have symptoms of hypothyroidism, so this disorder can be diagnosed on the basis of biochemical profile. [27] Secondly it is necessary to measure the serum TSH in patients who have constant nonspecific complaints particularly in the middle aged and older women. Finally, early detection of SCH is important to prevent progression of the disease to life threatening manifestations because SCH has shown increased morbidity due to hyperlipidemia especially in the middle-aged women. [2] Since SCH is more common in women and also due to its high prevalence, unless proper evaluation of TFT are done among the patients above 40years we are bound to miss the persons suffering from SCH. When the reproductive period is complete, females normally do not get much attention and health care from both the family as well as the neighborhood. Moreover, women at this age ignore certain signs and symptoms caused by thyroid dysfunction and they themselves consider these problems may be due aging or menopause. Thus, any

thyroid dysfunction if left unnoticed may end up in complications and further deteriorate the normal health and wellbeing of the individual. Hence thyroid profile should form an integral part in the evaluation of all the patients attending the outpatient department of various departments and then correction of thyroid dysfunction should be done at the earliest in order to prevent complications.

VI. Conclusion

Subclinical hypothyroidism which is also called reduced thyroid reserve is referred to as increased levels of serum thyroid stimulating hormone and fT3 and fT4 levels within normal limits⁶. The disease may be asymptomatic, but sometimes mild symptoms like weight gain, fatigue, constipation etc may be present. The present study aims to know the prevalence of SCH among perimenopausal women (40 to 55 years) and to study the relationship between SCH and cholesterol levels. We evaluated 60 patients who attended the medicine outpatient department and gynaecology outpatient department of SMIMS. The following parameters like age, blood pressure, pulse rate, height, weight, body mass index, fasting serum TSH, free T3, free T4 and cholesterol were collected. In our study prevalence of SCH in perimenopausal women (40 to 55 years) was 17% (10 patients affected out of 60 persons under study). In these patients who have been diagnosed to have SCH, 70% of the individuals had hypercholesterolemia and it has a statistically significant correlation with SCH.

The significant increase in the prevalence of SCH and its associated hypercholesterolemia is the major risk factor for atherosclerosis and myocardial infarction¹⁵. SCH has shown increased morbidity due to hyperlipidemia especially in the middle-aged women and most of them are not aware of the same², hence screening of perimenopausal women (40 to 55 years) with or without symptoms is mandatory for early diagnosis and treatment to prevent complications. It is concluded that perimenopausal women should be aggressively investigated for subclinical hypothyroidism irrespective of the signs and symptoms and treated before it progresses to overt hypothyroidism.

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