



## SUBCLINICAL HYPOTHYROIDISM IN METABOLIC SYNDROME AND ITS ASSOCIATION WITH LIPID PROFILE: A CROSS SECTIONAL STUDY FROM RAICHUR, KARNATAKA

### General Medicine

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### ABSTRACT

**Introduction:** It is estimated that one out of four people in the world suffer from Metabolic syndrome. There is a increase in prevalence of metabolic syndrome all over the world. Different regions are having individual clusters of epidemic risk factors and there is distinct evidence for high prevalence of metabolic syndrome in India and other South Asian countries. **Objective:** To study the association of subclinical hypothyroidism in metabolic syndrome and its association with lipid profile. **Materials and methods:** The present cross-sectional study was carried out from 1st February 2023 to June 30th 2023 including 103 cases attending the outpatient department and in-patients of Navodaya Medical college and Hospital, Raichur were taken. Data was analysed with SPSS and association with lipid profile was found out. Results: Out of 31 patients with SCH, majority were from 41-50 years age group i.e. 9(29%). Out of 31 patients with SCH, majority were females i.e. 17(54.8%). Elevated levels of TG in our study among SCH was 77.4%. Elevated levels of TC in our study among SCH was 32.3%. Elevated levels of LDL in our study among SCH was 29%. Reduced levels of HDL in our study among SCH patients was 58.1%. **Conclusion:** We found statistically significant association of subclinical hypothyroidism in metabolic syndrome with triglycerides ( $p < 0.05$ ).

### KEYWORDS

Subclinical Hypothyroidism, Metabolic Syndrome, Thyroid Dysfunction

Metabolic syndrome is a collection of factors which can increase the risk of heart disease, stroke and diabetes. Metabolic syndrome comprises of group of multiple risk factors for atherosclerotic cardiovascular disease (ASCVD) such as central obesity, hypertension, impaired fasting glucose (IFG) or type 2 diabetes mellitus (T2DM), elevated triglyceride levels (TG) and reduced high density lipoprotein cholesterol (HDL-C).<sup>1</sup> It is estimated that one out of four people in the world suffer from Metabolic syndrome.<sup>1</sup> There is a increase in prevalence of metabolic syndrome all over the world. Different regions are having individual clusters of epidemic risk factors and there is distinct evidence for high prevalence of metabolic syndrome in India and other South Asian countries.<sup>2-5</sup>

Subclinical hypothyroidism (SCH) is defined as a state of high serum TSH concentration and normal serum free / total thyroxine (T4), triiodothyronine (T3) concentrations associated with few or no symptoms / signs of hypothyroidism.<sup>6</sup> TSH concentration of more than 5 mIU/L and less than 10 mIU/L with a normal fT4 and fT3 concentration is taken as criteria for its diagnosis.<sup>7,8</sup>

Subclinical hypothyroidism is a state of mild thyroid failure. It is essentially a laboratory diagnosis. The patient should not have any classical signs/symptoms of hypothyroidism to label him/her as having subclinical hypothyroidism.<sup>9</sup>

There is a correlation between the changes seen in lipid profile and overt hypothyroidism. However, in cases of subclinical hypothyroidism the alteration in lipid profile is controversial where some studies have shown positive correlation and also the reversal of these changes after the patients received treatment while few studies suggest no significant correlation between the two entities. Moreover, there are only few Indian studies available regarding lipid profile changes in subclinical hypothyroidism.<sup>10,11,12</sup>

### OBJECTIVE

To study the association of subclinical hypothyroidism in metabolic syndrome and its association with lipid profile

### MATERIALS AND METHODS:

**Study Design:** Cross-sectional study.

**Study Period:** From 1<sup>st</sup> February 2023 to June 30<sup>th</sup> 2023

**Sample Size:** A total of 103 cases attending the outpatient department and in-patients of Navodaya Medical college and Hospital, Raichur were taken.

### Inclusion Criteria

- Age between 18-60 years
- Diagnosed cases of metabolic syndrome
- Those who are willing to participate in study after giving written consent

### Exclusion Criteria

- Past or present history of anti-thyroid drugs intake
- History of thyroid dysfunction including hypothyroidism, hyperthyroidism, goitre, thyroid malignancy Post thyroid surgery patients, external radiotherapy of neck
- Patient taking iodine or iodide containing drugs, CT contrast within 2 weeks, corticosteroids > 2 weeks within 3 months
- Pregnant woman
- History of chronic medical disorder including diabetes mellitus, end stage renal disease, cardiovascular disease, stroke, active liver disease and other autoimmune diseases
- Patients with acute medical illness admitted in ICU.

### Statistical Analysis And Methods-

Data was collected by using a structure proforma. Data thus was entered in MS excel sheet and analysed by using SPSS 24.0 version IBM USA. Qualitative data was expressed in terms of percentages and proportions. Quantitative data was expressed in terms of Mean and Standard deviation. Association between two qualitative variables was seen by using Chi square/ Fischer's exact test. A p value of <0.05 was considered as statistically significant whereas a p value <0.001 was considered as highly significant.

### RESULTS

**Table 1: Distribution according to age and gender**

|                    |       | Subclinical hypothyroidism |         |           |         | Total |
|--------------------|-------|----------------------------|---------|-----------|---------|-------|
|                    |       | Yes                        |         | No        |         |       |
|                    |       | Frequency                  | Percent | Frequency | Percent |       |
| Age group in years | 20-30 | 3                          | 9.7     | 11        | 15.3    | 14    |
|                    | 31-40 | 7                          | 22.6    | 17        | 23.6    | 24    |
|                    | 41-50 | 9                          | 29      | 14        | 19.4    | 23    |

|        |        |    |      |    |      |     |
|--------|--------|----|------|----|------|-----|
|        | 51-60  | 5  | 16.1 | 19 | 26.4 | 24  |
|        | 61-70  | 5  | 16.1 | 10 | 13.9 | 15  |
|        | > 70   | 2  | 6.5  | 1  | 1.4  | 3   |
|        | Total  | 31 | 100  | 72 | 100  | 103 |
| Gender | Male   | 14 | 45.2 | 48 | 66.7 | 62  |
|        | Female | 17 | 54.8 | 24 | 33.3 | 41  |
|        | Total  | 31 | 100  | 72 | 100  | 103 |

Out of 31 patients with SCH, majority were from 41-50 years age group i.e. 9(29%) followed by 7 i.e. 22.6% from 31-40 years age group and 5 each i.e. 16.1% from 51-60- and 61-70-years age group. Out of 31 patients with SCH, majority were females i.e. 17(54.8%) and remaining i.e. 14(45.2%) were males.

**Table 2: Distribution of SCH according to TG**

|    |          | Subclinical hypothyroidism |         |           |         | Total |
|----|----------|----------------------------|---------|-----------|---------|-------|
|    |          | Yes                        |         | No        |         |       |
|    |          | Frequency                  | Percent | Frequency | Percent |       |
| TG | Normal   | 7                          | 22.6    | 32        | 44.4    | 39    |
|    | Elevated | 24                         | 77.4    | 40        | 55.6    | 64    |
|    | Total    | 31                         | 100.0   | 72        | 100.0   | 103   |

Chi square-4.4 p-.036 (<0.05), Significant

Elevated levels of TG in our study among SCH was 77.4% compared to 55.6% of normal patients. The difference in the proportion of abnormal TG between SCH and normal subjects was found to be statistically significant (p<0.05). It means TG was high in SCH patients as compared to normal subjects with metabolic syndrome

**Table 3: Distribution of SCH according to TC**

|    |          | Subclinical hypothyroidism |         |           |         | Total |
|----|----------|----------------------------|---------|-----------|---------|-------|
|    |          | Yes                        |         | No        |         |       |
|    |          | Frequency                  | Percent | Frequency | Percent |       |
| TC | Normal   | 21                         | 67.7    | 58        | 80.6    | 79    |
|    | Elevated | 10                         | 32.3    | 14        | 19.4    | 24    |
|    | Total    | 31                         | 100.0   | 72        | 100.0   | 103   |

Chi square-1.9, p-0.15 (>0.05), Not Significant

Elevated levels of TC in our study among SCH was 32.3% compared to 19.4% of normal patients. The difference in the proportion of abnormal TC between SCH and normal subjects was found to be statistically not significant (p>0.05).

**Table 4: Distribution of SCH according to LDL**

|     |          | Subclinical hypothyroidism |         |           |         | Total |
|-----|----------|----------------------------|---------|-----------|---------|-------|
|     |          | Yes                        |         | No        |         |       |
|     |          | Frequency                  | Percent | Frequency | Percent |       |
| LDL | Normal   | 22                         | 71.0    | 50        | 69.4    | 72    |
|     | Elevated | 9                          | 29.0    | 22        | 30.6    | 31    |
|     | Total    | 31                         | 100.0   | 72        | 100.0   | 103   |

Chi square-0.027, p-0.87 (>0.05), Not Significant

Elevated levels of LDL in our study among SCH was 29% compared to 30.6% of normal patients. The difference in the proportion of abnormal LDL between SCH and normal subjects was found to be statistically not significant (p>0.05).

**Table 5: Distribution of SCH according to HDL**

|     |         | Subclinical hypothyroidism |         |           |         | Total |
|-----|---------|----------------------------|---------|-----------|---------|-------|
|     |         | Yes                        |         | No        |         |       |
|     |         | Frequency                  | Percent | Frequency | Percent |       |
| HDL | Reduced | 18                         | 58.1    | 38        | 52.8    | 56    |
|     | Normal  | 13                         | 41.9    | 34        | 47.2    | 47    |
|     | Total   | 31                         | 100.0   | 72        | 100.0   | 103   |

Chi square-0.24, p-0.62 (>0.05), Not Significant

Reduced levels of HDL in our study among SCH patients was 58.1% compared to 52.8% of normal patients of metabolic syndrome. The difference in the proportion of abnormal HDL between SCH and normal subjects was found to be statistically not significant (p>0.05).

## DISCUSSION

### Age and gender in SCH:

Out of 31 patients with SCH, majority were from 41-50 years age group i.e. 9(29%) followed by 7 i.e. 22.6% from 31-40 years age group

and 5 each i.e. 16.1% from 51-60- and 61-70-years age group. Out of 31 patients with SCH, majority were females i.e. 17(54.8%) and remaining i.e. 14(45.2%) were males.

**Khalid S Aljabri et al<sup>13</sup>** observed SCH to be more common in females than male patients (74.4 % vs. 25.6%, p = 0.009). Our study findings are in agreement with **Uzunulu et al<sup>14</sup>** and **Meng. et al<sup>15</sup>** and this has been observed in a number of studies including the general population. This is attributed to the higher iodine requirements in females; moreover, changes in reproductive hormones also cause changes in thyroid hormone levels. In addition, some females develop autoimmune antibodies to thyroid during pregnancy which causes postpartum subacute thyroiditis and can increase the risk of developing permanent hypothyroidism.<sup>12</sup> In the present study, SCH was more common in the age group 41-50 years which is previously reported and in concordance with **Singh et al.<sup>16</sup>** **Bermudez V et al<sup>17</sup>** also reported that common age group of SCH was 40-60 years with 26% prevalence of SCH in his study. **Senthil N et al<sup>18</sup>** also stated in age wise distribution of all cases, subclinical hypothyroidism is the most prevalent thyroid dysfunction in all age groups. Subclinical hypothyroidism is seen in 1.45% in 31-40 and 2.6 % in the 41 to 50 age group, none in the 51 to 60 years. They also reported that subclinical hypothyroidism is slightly higher in males (39%) in the age group of 40-50 years compared to the females.

### Association Of Subclinical Hypothyroidism In Metabolic Syndrome And Its Association With Lipid Profile

Elevated levels of TG were observed in 64 i.e. 62.1% patients. Elevated levels of TC were observed in 24 i.e. 23.3% patients. Elevated levels of LDL were observed in 31 i.e. 30.1% patients. Reduced levels of HDL were observed in 56 i.e. 54.4% patients.

In our study, elevated levels of TG among SCH was 77.4%, TC in 32.3%, LDL in 29% and reduced levels in HDL in 58.1%. **Bermudez V et al<sup>17</sup>** reported high triglycerides in 14.6% of SCH, low HDL in 11.1% of SCH patients in his study. Similarly, **Pesic et al<sup>19</sup>** in a case control study with 120 subjects, observed higher BMI, blood pressure, total cholesterol, serum TG, serum insulin, hypertension, and lower HDL-C levels in patients with SCH. **Senthil N et al<sup>18</sup>** reported in his study that out of 300 patients included in this study, 228 patients had abnormal triglyceride levels (76% of study group) and 215 patients had low HDL values (71%). **Punia et al<sup>20</sup>** investigated the prevalence of metabolic variable in metabolic syndrome and associated thyroid dysfunction. Of the 360 patients included in the study 62% had high values and 83 % had a low HDL. **Jayakumar et al<sup>21</sup>** in his study of thyroid status in metabolic syndrome included 120 patients. Of which 72 patients had low HDL (60% of study group) and 67 had high triglycerides - 56 % of the study group.

## CONCLUSION

We found statistically significant association of subclinical hypothyroidism in metabolic syndrome with triglycerides (p<0.05). The difference in the proportion of abnormal TC between SCH and normal subjects was found to be statistically not significant (p>0.05). The difference in the proportion of abnormal LDL between SCH and normal subjects was found to be statistically not significant (p>0.05). The difference in the proportion of abnormal HDL between SCH and normal subjects was found to be statistically not significant (p>0.05).

## REFERENCES

1. Tehrani FR, Tohidi M, Dovom MR, Azizi F. A population-based study on the association of thyroid status with components of the metabolic syndrome. *J Diabetes Metab.* 2011;2:156–162. doi:10.4172/2155-6156.1000156.
2. Misra A, Khurana L. The metabolic syndrome in South Asians: epidemiology, determinants, and prevention. *Metab Syndr Relat Disord.* 2009;7:497–514.
3. Sharma SK, Ghimire A, Radhakrishnan J, Thapa L, Shrestha NR, Paudel N et al. Prevalence of hypertension, obesity, diabetes, and metabolic syndrome in Nepal. *Int J Hypertens.* 2011;2011:821-971.
4. Misra A, Misra R, Wijesuriya M, Banerjee D. The metabolic syndrome in South Asians: continuing escalation & possible solutions. *Indian J Med Res.* 2007;125:345–54.
5. Wong ND, Sciammarella MG, Polk D, Gallagher A, Miranda-Peats L, Whitcomb B et al. The metabolic syndrome, diabetes, and subclinical atherosclerosis assessed by coronary calcium. *J Am Coll Cardiol.* 2003;41:1547–53.
6. Alejandro R. Ayala, Mark D. Danese, Paul W. Ladenson. When to treat mild hypothyroidism. *Endocrinology and metabolism clinics of North America.* 2000; 29 :399-415
7. Jameson JL, Mandel SJ, Weetman AP. Disorders of the thyroid gland 19<sup>th</sup> ed Vol 2 Harrison's principles of internal medicine 2015:2283-308
8. Brent GA, Weetman AP. Hypothyroidism and thyroiditis. 13<sup>th</sup> ed William's textbook of Endocrinology 2016: 439.
9. Cooper DS, Subclinical hypothyroidism. *JAMA.* 1987; 258: 246-7.
10. Atthans BU, Staub JJ, Ryff-de-lechel. LDL/HDL changes in subclinical hypothyroidism: possible risk factor for coronary heart disease. *Clin Endocrinol (oxf).* 1988;28:157-63.

11. Monzani F, Caraccio N, Kozáková M et al. Effect of levothyroxine replacement on lipid profile and intima media thickness in subclinical hypothyroidism. a double-blind placebo-controlled study. *J Clin Endocrinol Metab.* 2004;89:2099–106.
12. Hueston WJ, Pearson WS. Subclinical hypothyroidism and the risk of hypercholesterolemia. *Ann Fam Med.* 2004;2(4):351–5.
13. Khalid S Aljabri., Ibrahim M Alnasser, Samia A Bokhari, Muneera A Alshareef, Patan M Khan, Abdulla M Mallisho et al. "The Prevalence of Subclinical Hypothyroidism in Patients with Metabolic Syndrome in Saudi Community based Hospital: A Retrospective Single Centre Study". *EC Diabetes and Metabolic Research* 3.2 (2019): 44-9.
14. Uzunlulu M, Yorulmaz E, Oguz A. Prevalence of subclinical hypothyroidism in patients with metabolic syndrome. *Endocr J.* 2007;54:71–6.
15. Meng Z, Liu M, Zhang Q, Liu L, Song K, Tan J, Jia Q, Zhang G, Wang R, He Y, Ren X. Gender and age impacts on the association between thyroid function and metabolic syndrome in Chinese. *Medicine.* 2015 Dec;94(50).
16. Singh BM, Goswami B, Mallika V. Association between insulin resistance and hypothyroidism in females attending a tertiary care hospital. *Indian journal of clinical Biochemistry.* 2010 Apr 1;25(2):141–5
17. Bermudez V, Salazar J, Añez R, Rojas M, Estrella V, Ordoñez M, Chacín M, Hernández JD, Arias V, Cabrera M, Cano-Ponce C. Metabolic Syndrome and Subclinical Hypothyroidism: A Type 2 Diabetes-Dependent Association. *Journal of thyroid research.* 2018;2018.
18. Senthil N, Sneha T, Santhosh P, Sujatha S. A study of prevalence of thyroid dysfunction in patients with metabolic syndrome. *Int J Res Med Sci* 2015;3:3171–6
19. Pesic M. M., Radojkovic D., Antic S., Kocic R., Stankovic-Djordjevic D. Subclinical hypothyroidism: Association with cardiovascular risk factors and components of metabolic syndrome. *Biotechnology & Biotechnological Equipment.* 2015;29(1):157–163. doi: 10.1080/13102818.2014.991136.
20. Punia VPS. Study of metabolic syndrome and associated thyroid dysfunction in an urban population. *JIACM.* 2010;11(3):184–6.
21. Jayakumar RV. Hypothyroidism and metabolic syndrome. *Thyroid Res Pract.* 2013;10:1–2