

Thyroid Dysfunction in a Rural Region of North Kerala, India-Its Association with Dyslipidemia and Diabetes Mellitus

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ABSTRACT

The principle aim of our study was (i) to assess the thyroid status of this region and (ii) to study the relationship of thyroid dysfunction with Dyslipidemia and Diabetes Mellitus. Thyroid dysfunction was seen in 10.6% of the total 650 subjects with hypothyroidism in 8.6% subjects and hyperthyroidism in 2%. 46% of subjects with hyperthyroidism were in the age group 35-44 years and 32% with hypothyroidism in the age group 45-54 years. A higher percentage of women was both hypothyroid (13.2%) and hyperthyroid (2.3%) ($p=0.000$). 58% of women with hypothyroidism were in the age group 45-64 years and men in the age group 45-54 years. The majority of men with hyperthyroidism (50%) and women (57%) were in the age group 35-44 years. No significant association between TSH levels and economic status, diet and life style was observed. The total cholesterol levels were higher in the hypothyroid group whereas the LDL cholesterol was slightly increased in the hyperthyroid group. Women had higher serum total cholesterol levels across all three thyroid states as compared to men. 12.5% of hypothyroids and 24.2% of hyperthyroids had associated diabetes mellitus. Hypothyroidism is predominantly present, principally amongst women in this region and in the age group 45-64 years. Associated dyslipidemia and diabetes mellitus was also higher in this group. Early screening and treatment can help prevent possible cardiovascular outcomes.

Key Words: thyroid dysfunction, dyslipidemia, diabetes mellitus.

INTRODUCTION

Diseases of the thyroid gland are amongst the most abundant endocrine disorder in the world second only to diabetes mellitus. [1] The prevalence and pattern of thyroid disorders depends on sex, age, ethnic and geographical factors and especially on iodine intake. [2] A high iodine intake is associated with lower prevalence of goiter and higher prevalence of hypothyroidism whereas low intake is associated with a higher prevalence of hyperthyroidism. [3] The total burden of thyroid disorders in India is 42 million. This

projection was based on nationwide studies on thyroid disorders among adolescents and young adults. [4] Hypothyroidism has been reported to be more common in older women and ten times more common in women than men. [5] Prevalence of hyperthyroidism is also reported to be more common in women than men. [6]

Thyroid disorders are known to influence lipid metabolism. Overt and subclinical hypothyroidism has an adverse effect on serum lipid profile that may predispose to the development of atherosclerotic disease. [7] The association

between diabetes mellitus and thyroid dysfunction is well known. However the reported prevalence of thyroid dysfunction and associated diabetes mellitus varies with population diversity.^[8] There is a paucity of data from this region of Kerala. Our principle aim was (a) to assess the thyroid status of this region, (b) to study the relationship of abnormal thyroid function and abnormal serum lipid concentrations (c) to study the relation of thyroid dysfunction and Diabetes mellitus.

MATERIALS AND METHODS

This is a retrospective hospital based study. 650 subjects, (both male and female) who attended the “Sampoorna Arogya Project”, – a health scheme of Malabar Medical College Hospital and Research Centre during the period November 2012 to March 2013 formed part of the study group. Their age ranged from 18 to 80 years. The medical history, demographic details and anthropometric measurements were recorded in the patient data sheet. The lab investigations included fasting and post prandial blood sugar levels, lipid profile and measurement of TSH levels.

Inclusion criteria – subjects above the age of 18 yrs were included in the study.

The study was approved by the ethical committee of Malabar Medical College Hospital & Research Centre.

LAB INVESTIGATIONS:

Blood samples were collected by anterior cubital fossa venepuncture. They were requested to fast for 12 hrs prior to having their blood drawn.

TSH:

Levels of TSH were estimated quantitatively using the Enzyme Linked Fluorescent Assay (ELFA) technique on the Minividas Analyzer (Biomerieux, France). The analytical detection limit was 0.05 μ IU/ml, the laboratory's reference values for TSH = 0.25. – 5.0 μ IU/ml.^[9]

FASTING AND POST PRANDIAL BLOOD SUGAR:

It was estimated by the glucose oxidase peroxidase method (GOD-POD).^[10]

Cholesterol was estimated by the cholesterol oxidase peroxidase method (CHOD-PAP).^[11]

LDL cholesterol was calculated using the Friedwald's formula, LDL cholesterol = total cholesterol - (triglycerides/5 + HDL). Triglycerides were estimated by the glycerol phosphate oxidase peroxidase method (GPO-PAP).^[12] HDL cholesterol was estimated by a direct method.^[13]

The estimation of the above parameters was carried out on the fully automated analyzer EM 360 (Transasia Biomedicals Ltd, Erba Mannheim, Germany).

DATA ANALYSIS:

The thyroid status was defined as follows,

Hypothyroid – TSH levels $\geq 5.0\mu$ IU/ml

Hyperthyroid- TSH levels $\leq 0.25 \mu$ IU/ml

STATISTICAL ANALYSIS: was done using Microsoft Office “Excel” and Windows 10 operating system. We have analyzed with the IBM SPSS 21.0 statistical software package.

RESULTS

The 650 total subjects had an average range of 20-80 years. The highest number 29.4% were in the age group 45-54 years (figure 1). 53.4% were males and 46.6% females (figure 2). 40.9% subjects were housewives, 15.5% labourers and 10.9% Businessmen (figure 3). 83.7% were above the poverty line (APL). 98.5% were non-vegetarians and 76.9% had an active life style (figure 4).

THYROID FUNCTION TESTS:

Based on the above definition of thyroid status abnormal TSH concentration was found in 10.6 % of subjects (figure 5). An elevated TSH concentration (hypothyroidism) was seen in 8.6% subjects. A low TSH concentration (hyperthyroidism) was seen in 2% of subjects. The highest numbers of subjects with hyperthyroidism (46%) were seen in the age group 35-44 years (table 1). The

highest numbers of subjects with hypothyroidism were seen in the age groups 45-54 years (32%) and 55-64 years (27%). This was statistically significant ($p=0.002$) (Table 1).

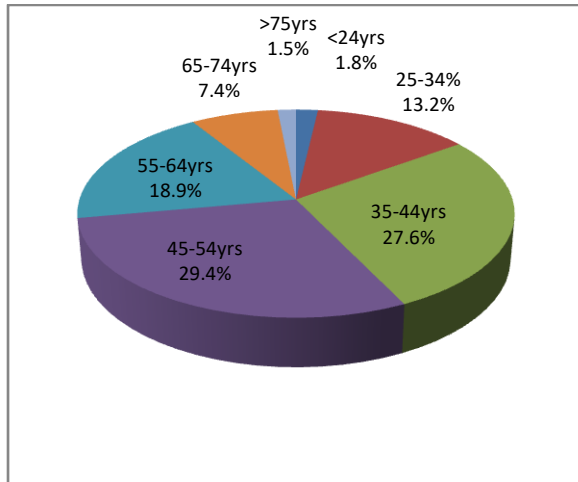


Figure 1: Age wise distribution of the subjects:

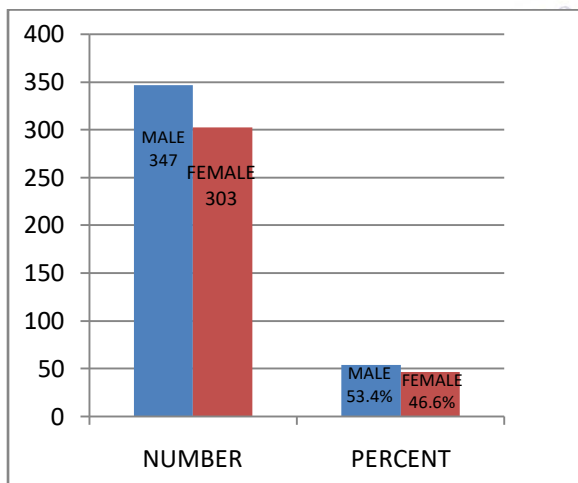


Figure 2: Gender wise distribution of subjects:

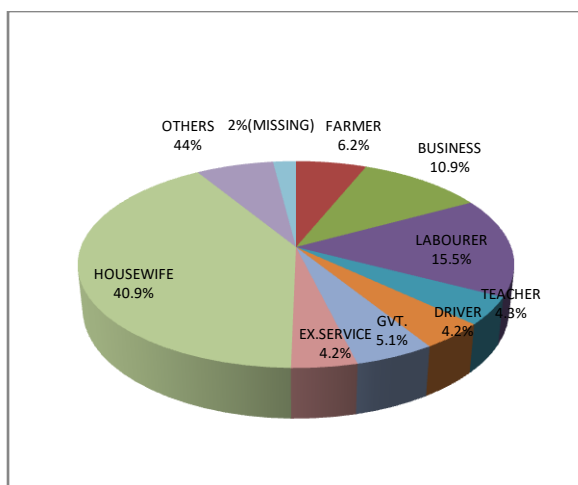


Figure 3: Distribution of Study Group as Per Occupation

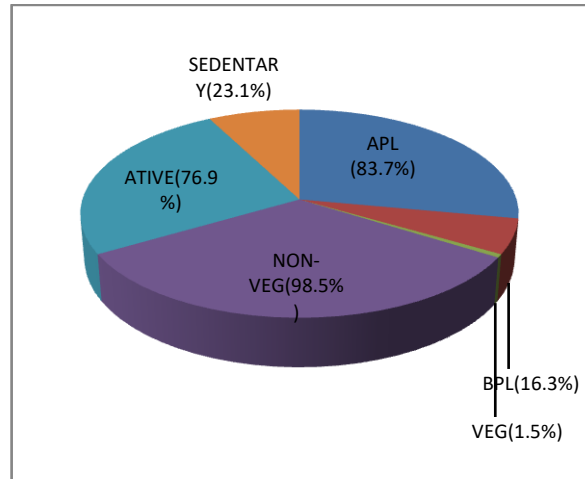


Figure 4: Other demographic details of the study group:

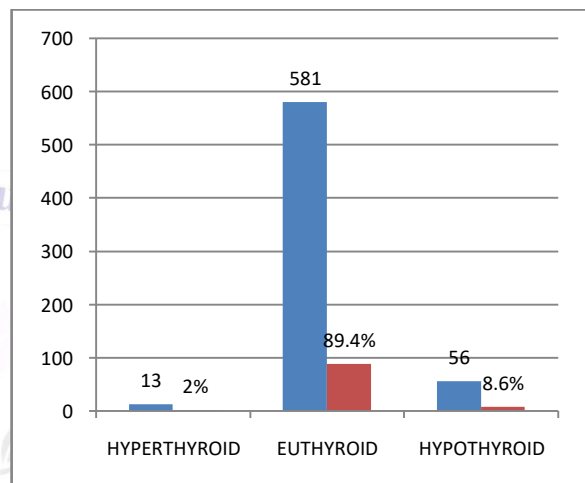


Figure 5: Thyroid status in the study group:

Men were more euthyroid than women (93.6% vs 84.0%). The percentage of women who were hypothyroid was 13.2% as against 4.6% for men. The percentage of women with hyperthyroidism was also greater as compared to men (2.3% vs. 1.7%). This was statistically significant ($p=0.000$). (Table 2) The majority of women with hypothyroidism (58%) was seen in the age group 45-64 years and the majority of men (44%) were in the age group 45-54 years (table 3). The majority of men with hyperthyroidism (50%) and women (57%) were in the age group 35-44 years. (table 4). The thyroid status was also analyzed as per the occupation of the study group. 14.6% of housewives were hypothyroid. This was not statistically significant ($p=0.063$) (Table 5). There was no statistically significant difference in thyroid

status between the two economically different study groups (Table 6). Thyroid dysfunction was seen mainly amongst those on a non-vegetarian diet (Table7). This was not statistically significant as the number of vegetarians was low. The life style of the study group did not significantly affect the thyroid status (Table 8).

Table 1: Thyroid Status at Different Age Groups

| Age group | Thyroid status | | |
|--------------|----------------|------------|-------------|
| | Hyperthyroid | Euthyroid | Hypothyroid |
| <24yrs | 1 | 11 | 0 |
| 25-34yrs | 1 | 78 | 7 |
| 35-44yrs | 6 | 164 | 10 |
| 45-54yrs | 0 | 173 | 18 |
| 55-64yrs | 3 | 105 | 15 |
| 65-74yrs | 0 | 43 | 5 |
| >75yrs | 2 | 7 | 1 |
| Total | 13 | 581 | 56 |

P value = 0.002

Table 2: Gender wise distribution of the thyroid status in the study group:

| Thyroid status | Male | | Female | |
|---------------------|--------|---------|--------|---------|
| | Number | Percent | Number | Percent |
| Hyperthyroid | 6 | 1.7 | 7 | 2.3 |
| Euthyroid | 325 | 93.6 | 256 | 84 |
| Hypothyroid | 16 | 4.6 | 40 | 13.2 |

P value= 0.000

Table 3: Distribution of hypothyroidism amongst men and women at different age groups

| AGE GROUP | GENDER | | TOTAL |
|------------------|-----------|-----------|-----------|
| | MALE | FEMALE | |
| 25.0-34.0 | 0 | 7 | 7 |
| 35.0-44.0 | 3 | 7 | 10 |
| 45.0-54.0 | 7 | 11 | 18 |
| 55.0-64.0 | 3 | 12 | 15 |
| 65.0-74.0 | 3 | 2 | 5 |
| 75.0+ | 0 | 1 | 1 |
| TOTAL | 16 | 40 | 56 |

P value= 0.213

Table 4: Distribution of hyperthyroidism amongst men & women at different age groups

| AGE GROUP | GENDER | | TOTAL |
|------------------|----------|----------|-----------|
| | MALE | FEMALE | |
| 25.0-34.0 | 1 | 0 | 1 |
| 35.0-44.0 | 3 | 4 | 7 |
| 45.0-54.0 | 0 | 0 | 0 |
| 55.0-64.0 | 2 | 1 | 3 |
| 65.0-74.0 | 0 | 2 | 2 |
| 75.0+ | 0 | 0 | 0 |
| TOTAL | 6 | 7 | 13 |

P value= 0.292

Table 5: Thyroid status as per occupation:

| OCCUPATION | Hyperthyroid | Euthyroid | Hypothyroid |
|-------------------|--------------|-----------|-------------|
| FARMER | 0 | 38 | 2 |
| BUSINESS | 2 | 65 | 4 |
| LABOURER | 2 | 93 | 6 |
| TEACHER | 0 | 27 | 1 |
| DRIVER | 0 | 26 | 1 |
| GOVT | 0 | 31 | 2 |
| EX.SERVICE | 1 | 25 | 1 |
| HOUSEWIFE | 7 | 220 | 39 |
| OTHERS | 1 | 43 | 0 |

P value= 0.063

Table 6: Thyroid status as per different economic status:

| | APL | BPL |
|---------------------|-----|-----|
| HYPERTHYROID | 10 | 3 |
| EUTHYROID | 488 | 93 |
| HYPOTHYROID | 46 | 10 |

P value – Not significant (0.751)

Table 7: Thyroid status as per diet:

| | Vegetarian | Nonvegetarian |
|---------------------|------------|---------------|
| HYPERTHYROID | 0 | 13 |
| EUTHYROID | 10 | 571 |
| HYPOTHYROID | 0 | 56 |

P value not significant (0.547)

Table 8: Thyroid status as per the life style of the subjects:

| | ACTIVE | SEDENTARY |
|---------------------|--------|-----------|
| HYPERTHYROID | 11 | 2 |
| EUTHYROID | 444 | 137 |
| HYPOTHYROID | 45 | 11 |

P value not significant (0.641)

SERUM LIPID CONCENTRATIONS:

The total cholesterol level was higher in the hypothyroid group as compared to the euthyroid and hyperthyroid group with a down ward trend across the three thyroid status. The triacylglycerol and HDL levels were within the normal range in all three states. LDL levels were within the normal range in the hypothyroid and euthyroid subjects but were slightly increased in the hyperthyroid subjects (Table 9). Women had higher serum total cholesterol levels across all three thyroid states as compared to men. On the other hand triacylglycerol levels were lower in women as compared to men across the three thyroid states. This data was not statistically significant. (Table 10)

DIABETES:

8.3% of total subjects were pre-diabetic and 13.9% diabetic (Table 11). 5.5% of men were pre-diabetic and 8.2% diabetic as compared to 2.8% women (pre-diabetic) and 5.7% women (diabetic) (Table 12). 7.1 % of hypothyroids were pre-diabetic and 12.5% diabetic. 7.1% of hyperthyroids were pre-diabetic and 24.4% had diabetes (Table 13). Amongst 7 diabetics in the hypothyroid group 3 were women and amongst the 3 diabetics in hyperthyroid group, 3 were women. This distribution was not statistically significant (Table 14).

Table 9: Mean levels of total cholesterol (TC), Triglycerides (TG), High Density Lipoprotein (HDL) and Low Density Lipoprotein (LDL) at different thyroid states.

| THYROID STATUS | TC | TG | HDL | LDL |
|----------------|-------|-------|------|-------|
| HYPOTHYROID | 210.4 | 113.3 | 43.5 | 144.2 |
| EUTHYROID | 204.8 | 114.5 | 43.3 | 139.6 |
| HYPERTHYROID | 195 | 91.7 | 43.5 | 179 |

Table 10: Gender wise Distribution Of thyroid Status & Their Mean Lipid Levels

| | | TC | TG | HDL | LDL |
|--------------|--------|-----|-----|-----|-----|
| HYPOTHYROID | Male | 207 | 127 | 43 | 139 |
| | Female | 212 | 108 | 44 | 147 |
| EUTHYROID | Male | 201 | 130 | 43 | 138 |
| | Female | 210 | 95 | 44 | 142 |
| HYPERTHYROID | Male | 183 | 111 | 45 | 192 |
| | Female | 208 | 79 | 42 | 149 |

P value not significant

Table 11: Status of diabetes:

| DIABETES STATUS | NUMBER | PERCENT |
|-----------------|--------|---------|
| NORMAL | 506 | 77.8 |
| PREDIABETIC | 54 | 8.3 |
| DIABETIC | 90 | 13.9 |

Table 12: Status of diabetes in the study group amongst males & females:

| DIABETES STATUS | Male | | Female | |
|-----------------|--------|------|--------|------|
| | Number | % | Number | % |
| NORMAL | 258 | 39.7 | 248 | 38.1 |
| PREDIABETIC | 36 | 5.5 | 18 | 2.8 |
| DIABETIC | 53 | 8.2 | 37 | 5.7 |

Table 13: States of diabetes and thyroid function in the study group:

| THYROID STATUS | NORMAL BLOODSUGAR | | PREDIABETIC | | DIABETIC | |
|----------------|-------------------|------|-------------|-----|----------|------|
| | Number | % | Number | % | number | % |
| HYPOTHYROID | 45 | 80.4 | 4 | 7.1 | 7 | 12.5 |
| EUTHYROID | 452 | 77.8 | 49 | 8.4 | 80 | 13.8 |
| HYPERTHYROID | 9 | 69.2 | 1 | 7.1 | 3 | 24.4 |

Table 14: Gender wise distribution of diabetes & thyroid function in the study group:

| THYROID STATUS | GENDER | NORMAL | PREDIABETIC | DIABETIC | P VALUE |
|----------------|--------|--------|-------------|----------|---------|
| HYPOTHYROID | MALE | 11 | 1 | 4 | 0.121 |
| | FEMALE | 35 | 3 | 3 | |
| EUTHYROID | MALE | 243 | 34 | 49 | 0.08 |
| | FEMALE | 209 | 15 | 31 | |
| HYPERTHYROID | MALE | 5 | 1 | 0 | 0.09 |
| | FEMALE | 4 | 0 | 3 | |

DISCUSSION

From this study abnormal TSH concentration was seen in 10.6% of subjects. The Colorado study [14] reported 11.7% subjects with abnormal TSH concentration which is close to what we have obtained from our study. In a cross sectional surveys in central Kerala Usha et al. have reported thyroid function abnormalities in 19.6% of population. [15] The prevalence of thyroid dysfunction among young females in a South Indian population was 12.5%. [16] In an earlier study on the prevalence of thyroid disorders in women of Pondicherry 15.8% had thyroid dysfunction. [17]

An elevated TSH concentration (hypothyroidism) was seen in 8.6% of subjects. This is within the range seen in literature and is consistent with other findings in an iodine replete population. [14-17] A low TSH concentration (hyperthyroidism) was seen in 2% of subjects. The prevalence of hyperthyroidism has been reported in several studies. In an

epidemiological study from Cochin, subclinical and overt hyperthyroidism was present in 1.6% and 1.3% of subjects participating in a community Survey. [15] In a hospital based study of women from Pondicherry hyperthyroidism was seen in 1.8% of subjects. [17] In another study from South India low TSH was seen in 1.5% of young females. [16] Our values are very similar to the Colorado study [14] where 2.2% of their subjects had TSH<0.3 µIU/ml. In the Wickham Survey thyrotoxicosis was seen in 1.6% of the total subjects. [18] In more recent reports Hoogendorn reported thyrotoxicosis in 1.2% subjects [19] and Hallowell et al. in their (NHANES III) study an incidence of 1.3%. [20]

In our study the percentage of subjects with high serum TSH concentration was higher in women (13.2%) than men (4.6%). This has been corroborated by other studies. [14,21- 22] The percentage of subjects with hyperthyroidism was also greater in women (2.3%) as compared to men (1.7%). The highest proportion of subjects with

hypothyroidism was seen in the age group 45-54 years (27.5%) and 55-64 yrs (50%). A number of papers have reported an elevated TSH level with advancing age particularly in women. [17, 20-21] Interestingly 44% of men with hypothyroidism was in the age group 45-54yrs (table 3). The majority of men (50%) and women (57%) with hyperthyroidism were seen in the age group 35-44yrs. Hyperthyroidism (62%) was largely seen in the age group 45 years and below. (table 4) Only 0.8% of total subjects who had hyperthyroidism were above the age of 45 years. Other reports have given a prevalence value of 2% in the elderly. (22, 23)

SERUM LIPID CONCENTRATION:

Thyroid disorders are known to influence lipid metabolism. Hypothyroidism is most frequently associated with disorders of lipid metabolism. The total cholesterol level was higher in the hypothyroid group as compared to the euthyroid and hyperthyroid groups (table 9). It has been reported that overt and subclinical hypothyroidism is associated with hypercholesterolemia. [14,24] The triacylglycerol and HDL levels were within the normal range. No significant change in serum TG and HDL has also been previously reported. [14] LDL levels were within the normal range in the hypothyroid and euthyroid subjects but were slightly increased in the hyperthyroid subjects. Other studies have reported an increase in LDL in overt hypothyroidism and a decrease in LDL and total cholesterol levels in hyperthyroidism. [24] We have observed a decrease in cholesterol in hyperthyroid subjects (table 9). This has been attributed to increased bile excretion of cholesterol. [25] Triacylglycerol levels were relatively decreased as compared to euthyroid and hypothyroid states but there was no change in HDL levels. Women had higher serum total cholesterol and LDL levels across all three states as compared to men (table10). This has also been observed by Canaris and co-workers in the Colorado study. [14]

THYROID STATUS AND DIABETES:

There is a deep underlying relationship between diabetes mellitus and thyroid dysfunction. Of the 90 patients who were diabetic 12.5% were hypothyroid and 24.4% were hyperthyroid. Makandar et al. [26] have reported 22% of diabetics to be hypothyroid and 10% to be hyperthyroid. The overall prevalence of diabetes in our study group was 13.9%. Palmer et al. [27] have reported an overall prevalence of 14.7% in their studies. Both Hypothyroidism and hyperthyroidism was more prevalent amongst female diabetics.

CONCLUSION

This is the first report of thyroid status in this region of north Kerala, India. 8.6% of total subjects were hyperthyroid and 2% of the total subjects were hypothyroid. A higher percentage of women were both hyperthyroid and hypothyroid. Hypothyroidism in women was more marked in the age group 45-64 years. Hyperthyroidism was mainly seen in the age group <45years. The total cholesterol level was higher in the hypothyroid group as compared to the hyperthyroid group with women having a higher total cholesterol level as compared to men. More number of men were diabetic as compared to women but more females with thyroid dysfunction had associated Diabetes mellitus.

The above data indicates that thyroid dysfunction, particularly in women and in the age group 45-64 years is very high in this region. Screening for thyroid disease should be considered mandatory during routine evaluation of this susceptible group. This should be followed with appropriate treatment as possible aggravation of classical risk factors such as hypertension and dyslipidemia can lead to an increased cardiovascular risk in these patients. Associated diabetes mellitus with thyroid dysfunction seen particularly in women also merits early detection and initiation of treatment.

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