Introduction

Thyroid disorders and Diabetes mellitus have a propensity to appear together due to an interaction between thyroid hormones and insulin. They have been shown to mutually influence each other and associations between both conditions have been reported previously. There is a higher prevalence of thyroid dysfunction in type 2 Diabetics than in the general population. Insulin and thyroid hormones are involved in cellular metabolism hence excess or deficit of either of these hormones could result in functional derangement of the other i.e. hyperthyroidism can result in hyperglycemia or hypothyroidism in hypoglycemia.

Unrecognized thyroid dysfunction may impair metabolic control i.e. glycemic control and lipid profile, by causing hypoglycemia or hyperglycemia and it can cause an additional cardiovascular disease risk in patients with Diabetes. A study was undertaken to find the prevalence, and distribution of thyroid disorders in type 2 diabetes mellitus, and to evaluate the relationship between glycemic control and occurrence of altered thyroid function in type 2 diabetes mellitus.

Material And Methods

The study was carried out at Basaveshwar Teaching and General Hospital, Kalaburgi, Karnataka from January 2015.
to May 2016. 150 patients with known type 2 diabetes mellitus or newly detected type 2 diabetes mellitus without known thyroid disorders were included in the study.

**Inclusion Criteria**
Known type 2 diabetes mellitus and newly detected type 2 diabetes mellitus with age >35 years

**Exclusion Criteria**
- Patients with known thyroid disease
- Patients with acute illness (sepsis, acute myocardial infarction, severe heart failure, recent admission in intensive care unit)
- Patients with hepatic dysfunction
- Patients with psychiatric illness.
- Pregnancy
- Patients on treatment with drugs interfering with thyroid function (amiodarone, propranolol, corticosteroids and oral contraceptives).

All patients in the study group were selected without any bias for sex, duration, severity or control of diabetes. A thorough history was recorded with particular emphasis on symptoms of hypothyroidism and hyperthyroidism. The presence of associated illness like coronary artery disease, hypertension and cerebrovascular accident were noted. Family history regarding diabetes mellitus and treatment history of oral hypoglycemic agents or insulin along with duration was also included.

A thorough general and systemic examination was carried out. The fundus examination for diagnosis of diabetic retinopathy and neurological examination for diabetic neuropathy were also done.

**BMI Calculation (quetelet Index):** Body mass index (BMI) is calculated with height and weight of the subject using the formula: BMI = weight (kg) / height (m)²

**Blood Sugar:** Both fasting and postprandial blood sugar are estimated by Tinder's (Glucose oxidase) method and read at 505/670 nm.

**Renal Function Test:** The Blood Urea in this study was estimated using DAM method (Diacetyl Monoxime). Serum creatinine was estimated using Modified Jaffe's method.

**Urineanalysis:** Urine sample is collected for urine routine analysis. The urine was examined for sugar, protein, cytology and urinary sediments.

**Fasting Lipid Profile:** Total cholesterol, Triglyceride (TGL), Low Density Lipoprotein (LDL) Cholesterol and High Density Lipoprotein (HDL) Cholesterol levels were analyzed on the early morning fasting Blood Sample.

**Methods Used:**
- Total cholesterol- CHOD POD METHOD
- HDLC -Selective immune precipitation method
- Triglycerides - Enzymatic calorimetric method
- LDLC - Derived from TC and TGL values.
- VLDL - Derived from triglyceride values.

**HbA1c:** Blood sample collected in EDTA coated tubes and HbA1c is estimated by Biorad-HPLC method.

**Thyroid Profile:** The estimation of FT3, FT4 and TSH were done on fasting serum sample and the methods used were as follows:
- TSH – Ultrasensitive 3rd generation sandwich chemiluminescent immunoassay by using Siemens ADVIA Centaur®CP/XP
- FT3 & FT4 - Competitive chemiluminescent immunoassay.

**Reference Values:**
- FT3: 0.7-3.5pg/ml, FT4: 0.8- 1.8 ng/dl
- TSH: 0.220-5.550mIU/ml

Various thyroid disorders were recognized when they exhibited the following abnormalities in the level of TSH, FT3 and FT4.

| Thyroid disorder       | TSH            | FT3   | FT4   |
|------------------------|----------------|-------|-------|
| Overt hypothyroidism   | >5.55 mIU/ml   | <0.7 ng/dL |
| Subclinical hypothyroidism | >5 mIU/ml     | normal | normal |
| Overt hyperthyroidism  | <0.22 mIU/ml   | >1.8 ng/dL  |
| Subclinical hyperthyroidism | <0.22 mIU/ml | normal | normal |

Statistical analysis was done by using Large Sample Z test, ANOVA and LEVENE’s Test and Co relation coefficient with t Test to know the significance by calculating p value.

**Results**

**Distribution of Cases According to Age and Sex**
The study sample included 150 patients with type 2 Diabetes mellitus

Distribution of the study sample according to age and sex is shown in Table 1.
In present study of 150 cases, 88 (58.66%) were males and 62 (41.33%) females. 107 (71.4%) were in the age group 41 to 60 years.

**Distribution of Cases According to Duration of Diabetes** (Table 2)

| Duration in years | No of cases | Percentage |
|-------------------|-------------|------------|
| 0-1               | 12          | 8.0        |
| 1-5               | 99          | 66.0       |
| 6-10              | 22          | 14.7       |
| >10               | 17          | 11.3       |
| Total             | 150         | 100.0      |

Mean ± SD 4.75 ± 3.80

99 (66%) had Diabetes over a period ranging from 1 to 5 years. 54 cases had a family history of diabetes mellitus and none had history of thyroid dysfunction in family. There were 81 (54%) cases of hypertension and 25 cases gave history of coronary artery disease in the past.

In the present study of 150 study samples 120 were on regular treatment either exogenous insulin or oral hypoglycemic agents. 122 cases among 150 were on OHAs and 19 on insulin and 9 cases were on both OHA and Insulin.

**Level of TSH in Different Variables in Diabetics** (Table 3).

In this study, there was no association to the abnormal thyroid levels to total leukocyte count and ESR of patients whereas neutrophilia and eosinophilia were found highly significant with p value more less than 0.05 and less than 0.001 respectively.

Abnormalities in FBS and HbA1c were found highly significant with p values less than 0.001 and 0.005 respectively, High PPBS was seen with abnormal TSH levels which was significant with p value being less than 0.05

**Level of TSH among Different Variables in Diabetics** (Table 4)

In this study of liver enzymes, SGPT was found abnormal
with thyroid abnormalities with p value less than 0.05 which is statistically significant. Serum Albumin levels were also found abnormal in cases with abnormal TSH levels which was also statistically significant with p value being less than 0.05. Serum Creatinine levels were found abnormal in six cases which had no correlation with abnormal thyroid levels.

### Thyroid Profile (Table 5)

| Thyroid profiles | Below normal | Normal | Above normal |
|------------------|--------------|--------|-------------|
| T3               | 2            | 122    | 16          |
| T4               | 2            | 122    | 16          |
| TSH              | 4            | 107    | 39          |

### Distribution of Thyroid Diseases in Diabetics (Table 6)

| Thyroid Profile | Number of Cases | Percentage (%) |
|-----------------|-----------------|----------------|
| Normal          | 107             | 71.33          |
| Overt Hypothyroidism | 16       | 10.67          |
| Sub clinical hypothyroidism | 23       | 15.34          |
| Overt Hyperthyroidism | 2       | 1.33           |
| Sub clinical hyperthyroidism | 2       | 1.33           |
| Total           | 150             | 100            |

Among 150 cases of Type 2 diabetes 43(28.67%) had abnormal thyroid functions. Of these 23(15.34%) had subclinical hypothyroidism 16 (10.66%) overt hypothyroidism and 2(1.33%) each had subclinical and overt hypothyroidism

### Thyroid Disorders with Demographic Profile (Table 7)

In the present study age, gender and socio economic status did not show any significant association with thyroid dysfunction (p value being more than 0.05). There was significant association between duration of disease and thyroid abnormalities

| Variables                | TSH MEAN ± SD | F-VALUE | P-VALUE | SIG. |
|--------------------------|---------------|---------|---------|------|
| Sex                      |               |         |         |      |
| MALE                     | 5.31±2.42     | F=1.042 | P>0.05  | NS   |
| FEMALE                   | 4.89±2.67     |         |         |      |
| Age                      |               |         |         |      |
| ≤50 YEARS                | 5.13±2.15     | F=1.86  | P>0.05  | NS   |
| >50 YEARS                | 5.38±2.64     |         |         |      |
| Socio-economic status    |               |         |         |      |
| HIGH                     | 5.39±1.93     | F=0.882 | P>0.05  | NS   |
| LOW                      | 5.13±2.53     |         |         |      |
| Duration                 |               |         |         |      |
| <5 YEARS                 | 5.06±2.34     | F=13.48 | P<0.001 | HS   |
| >5 YEARS                 | 5.70±2.19     |         |         |      |

### Discussion

Thyroid hormones are intimately involved in cellular metabolism. An excess or deficit of either insulin or thyroid...
hormone could result in the functional derangement of the cellular metabolism.

In the present study of 150 type 2 diabetic patients, 13 belonged to age group of 30 to 40 years, 43 to the age group of 41 to 50 years, 54 belonged to the age group of 51 to 60 years, 7 to the age group of 61 to 70 years, 19 to the group of 71 to 80 years and 4 were aged more than 80 years.

This observation was similar to World Health Organization (WHO) report which predicted that while the main increase in diabetes would be in the > 65 year age group in the developed countries, in India and developing countries the highest increase would occur in the age group of 45-65 year of age group. Kapur and coworkers have reported maximum number of cases between 40 and 59 year of age without any significant difference between the genders.

Duration of Diabetes Mellitus
In the present study, 99(66%) patients had disease duration between 1 to 5 years, and 22(14.7%) between 6 to 10 years. 17(11.3%) had disease duration >10. Majority of people were in the age group between 41 to 60 years and had duration of disease.

Co-morbid Diseases
In the present study, 54% of diabetics (81) of the studied had hypertension Tanow et al observed that 78% of IDDM patients and 50% of NIDDM had hypertension. Fuller and colleagues observed that the frequency of WHO defined hypertension was highest in NIDDM patients older than 53 years, and was noted in 43% of male and 52% of females. Both these studies support the findings of the present study.

In the present study, 16.7% (25 in number) of diabetic patients had coronary artery disease. Type 2 diabetes increases relative risk of cardiovascular disease two- to fourfold compared with the risk in the general population.

Family History of Diabetes Mellitus
In the present study, among the diabetics 36% (54) of patients had family history of Diabetes. Viswanathan and colleagues in a study 107 subjects found 73 giving a positive family history diabetes, 19 subjects (26%) later developed diabetes.

Regularity of Treatment
In the present study of 150 subjects, 9(6%) were newly detected Diabetics. 80% (120) of patients were on regular treatment and 14% (21) were irregular in their medication. Asha and colleagues in their study observed 97% of type 2 diabetics on anti-diabetic agents and most were using them irregularly. The compliance was 62% among the diabetics who were on oral anti-diabetic agents.

BMI
Among the study population, 28.7% (43) were overweight and 14% (21) obese; 55.3% (83) had normal BMI, 3 (2%) were underweight McLarty et al reported that prevalence of IGT in subjects of all age group increased with rising BMI. Yon Gik et al reported that the prevalence of diabetes mellitus and IGT increased with rising BMI and with increase in WHR, both these studies support study findings.

Retinopathy
In the present study, 19.3% (29) Diabetic patients had diabetic retinopathy. This study was almost like that of Southwell et al who found that prevalence of diabetic retinopathy was 15%.

Peripheral Neuropathy
None of the diabetic patients in our study had peripheral neuropathy.

Peripheral Vascular Disease
Of 150 diabetic patients 9 patients (6%) had peripheral vascular disease. Agarwal et al in their study observed that the prevalence of peripheral vascular disease in diabetic patients to be 14%.

Dyslipidemia
In the present study, 50% (75) patient had raised total cholesterol level; 84% (126) had raised triglycerides level; 44% (66) had decreased HDL-C level and 50% (75) had raised LDL-C levels. This shows that the incidence of dyslipidemia is high in diabetics. Liao et al reported that patients who had diabetic glycemic tolerance had more of intra-abdominal fat, higher triglyceride levels, lower HDL cholesterol levels and higher blood pressure than those with Normal glucose tolerance. Southwell et al in their study found that 40% of the diabetics exhibiting hypercholesterolemia. The above studies support our findings.

HbA1c Level
In the present study, 52% of diabetic (78) had HbA1c level more than 8 compared to 46% (69) who had level
HbA1c less than 8%. More than half of the diabetics had poor glycemic control only 2% or (3) had HbA1c<6. Paolo Fumelli et al in their study of 562 diabetic patients found that all patients have level of HbA1c greater than 8%.[19]

**Abnormal Thyroid Profile**

In the present study, 28.6% (43/150) of patients with diabetes mellitus had abnormal thyroid profile. Similar findings have been encountered by Laloo Demistrot and colleagues in Manipur, India.[20] They found prevalence of thyroid disease in 31.2% of 202 type 2 diabetic patients.

The present study showed higher prevalence of thyroid abnormalities. Abdel-Rahman et al in their study of 908 type 2 diabetic patients found prevalence of thyroid disease in 12.5% cases. 6.6% of whom were newly diagnosed and 5.9% had known thyroid dysfunction. The prevalence of thyroid disease in the non-diabetic control group was 6.6%.[21]

Chubb et al in a cross-sectional study of 420 patients with type 2 diabetes mellitus found that 8.6% of patients having subclinical hypothyroidism.[22] Smithson in his study found the prevalence of thyroid disease in 10.8% diabetic patients registered in the general practice. In the control group of non-diabetics, the prevalence was 6.6%.[23]

Akbar and colleagues in their study of 100 type 2 diabetics found that the prevalence of thyroid dysfunction was 16% and it was 7% in control group of non-diabetics.[24]

El Nobre et al in their study showed association between diabetes mellitus and abnormal thyroid profile to be like our finding.[25]

Zdrojewicz et al in their study of 75 diabetic patients found that there were no differences in thyroid gland function between patients with type 2 diabetes mellitus and non-diabetics. This study contradicts our findings.[26] Thakkar and Jain in their study found no significant correlation between type 2 diabetes and hypothyroidism.[27] This study findings contraindicates our study.

**Distribution of Thyroid Abnormalities**

In the present study, 15.34% (23/150) of the patients had subclinical hypothyroidism and 1.5% (2/150) of the patients sub clinical hyperthyroidism, and 10.67%(16) had overt hypothyroidism and 1.5%(2) had overt hyperthyroidism.

The results of the present study was similar to the results of Abdel-Rahman et al who in their study of 908 type 2 diabetic patients found that 10.3% of patients had hypothyroidism (overt and sub clinical) and 1.7% of patients had hyperthyroidism (overt and sub clinical).[21]

Smithson et al in their study of 233 diabetes mellitus patients found that 11 patients to have undiagnosed thyroid disease, out of which 9 were having hypothyroidism (overt and sub clinical) and 2 hyperthyroidisms (overt and sub clinical).[23]

**Significance of Age in Patients with Abnormal Thyroid Profile**

Among the patients in Diabetic group with abnormal thyroid profile, 23 (54%) were of age less than 50 years and 20 (46%) were of age more than 50 years showing no significant association of age with thyroid dysfunction.

**Significance of Duration of Diabetes and Abnormal Thyroid Profile**

In the present study of 43 cases 30(70%) had duration of diabetes more than 5 years which was statistically significant with p value being less than 0.001. The present study findings contradict with that of Chubb et al who in their study found that age and anti-TPO status to correlate with altered thyroid profile in diabetic patients.[22] Vondra et al found that thyroid diseases in diabetic patients is 2-3 times higher than in non-diabetic subjects; it raises with age, and is strongly influenced by female gender and autoimmune diabetes.[28] These results contradict with our findings.

**Conclusion**

Prevalence of thyroid dysfunction is common among patients with type 2 diabetes mellitus (28.66%). Hypothyroidism including subclinical hypothyroidism is common among them. The condition was noted among those having diabetes over a period of 5 years.

There is a significant correlation between abnormal thyroid profile and family history of diabetes, BMI and serum lipid profile. However no co relation exist between abnormal thyroid profile and age, gender and socio economic status of the patients.

There is significant co relation between diabetic control (FBS, PPBS and HBA1c) and abnormal thyroid profile. However, no relation is seen between complications of diabetes like retinopathy, peripheral vascular disease and neuropathy and thyroid dysfunction.

Routine screening for thyroid dysfunction in type 2 diabetes mellitus patients may be justified because the progression to overt thyroid dysfunction is associated with significant morbidity including the adverse effects on glycemic control, and lipid profile.
3rd generation TSH assay as routine screening in patients with Type 2 Diabetes Mellitus to know the status of Thyroid profile is helpful to assess the status and for further management to prevent progression of disease

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