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A Study Of Thyroid Dysfunction And Its Associated Risk Factors Among Type 2 Diabetes Mellitus Patients.

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ABSTRACT

Thyroid diseases and diabetes mellitus are the two most common endocrine disorders encountered in clinical practice. Both these disorders have been shown to mutually influence each other and relationships between both conditions have long been reported. Thyroid hormones play a vital role in the regulation of carbohydrate metabolism and pancreatic function, and on the other hand, diabetes mellitus affects thyroid hormone levels to variable extents. Thyroid disease must be screened annually in diabetic patients to detect asymptomatic thyroid dysfunction. Diabetes mellitus and thyroid dysfunction can be found to exist together where thyroid disease can affect glucose metabolism and the untreated thyroid dysfunction can affect the control of diabetes. The present study was intended to explore thyroid dysfunction and its associated risk factors among patients with type 2 diabetes mellitus. A cross-sectional study was conducted among patients with type 2 diabetes on treatment for 3 years with age group of more than 30 to 50 years and 100 patientstaken up for the study attending the outpatient department of Government Villupuram Medical College, Villupuram, Tamil Nadu. India . The assessment parameters for this study based on their life style factors and biochemical analysis such as FBS, PPBS, HbA1C, Lipid profile, Renal function test, Thyroid profile (ELISA).From the assessment status of diabetics, males have uncontrolled diabetes when compared to females and p value is <0.05 and it was statistically significant. Assessment of thyroid dysfunction in diabetics showed that males with thyroid dysfunction in the age group of 30-40 years are less when compared to females in the same age group. P value is <0.05 and is statistically significant. But incidence of thyroid dysfunction in type 2 DM is higher in the age group of 41-50 years in both genders when compared to age group of 30-40 years. Correlation between thyroid dysfunction and diabetes in males and females among various age groups showed that thyroid dysfunction in females is greater even if they have controlled diabetes when compared to males. But thyroid dysfunction in males with uncontrolled diabetes is higher than females with uncontrolled diabetes. Incidence of thyroid dysfunction in females is higher even if they have controlled diabetes. This may be linked with their reproductive age and p value is <0.05 and it is statistically significant. Comparison of incidence of renal failure in diabetics shows 8% of the males have renal failure and 4% of females have renal failure, indicates greater incidence of renal failure among males. Incidence of hypertriglyceridemia (triglycerides) is higher in males when compared to females and p value is <0.05 and it is statistically significant. Incidence of hypercholesterolemia (total cholesterol) is higher in females than males in the age group of 41-50 years and p value is <0.05and it is statistically significant. Co-incidence of thyroid dysfunction with hyperlipidemia is higher in male diabetic patients when compared to female diabetics. Assessment of Thyroid profile in the present study showed that thyroid dysfunction is greater in females even if they had controlled diabetes when compared to males. Thyroid dysfunction is higher in uncontrolled diabetic males when compared to females with uncontrolled diabetes. It seems that incidence of thyroid dysfunction is more in females even if they had controlled diabetes. This may be associated with their reproductive age. The present study showed that the prevalence of thyroid dysfunction among Indian diabetic patients attending an outpatient clinic was 12.3%.Co-incidence of thyroid dysfunction with hyperlipidemia and renal failure is higher in male diabetics when compared to female diabetics. Hence it is concluded that thyroid dysfunction is positively associated with hyperlipidemia and renal dysfunction in type 2 DM. Regular evaluation of thyroid profile, lipid, profile and renal parameters is highly beneficial in type 2 DM patients and regular treatment of thyroid dysfunction with hyperlipidemia may reduce the risk of development of cardiovascular and renal complications in type 2 DM patients. Further research is needed to elucidate the exact molecular mechanism behind the link between hyperlipidemia and thyroid hormone dysfunction in type2 DM and the life style modification also to be assessed.

Keywords: Thyroid dysfunction, type 2 DM. Thyroid hormones, Hyperlipidemia, renal parameters

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INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder that results in hyperglycemia (high blood glucose levels) due to being ineffective at using the insulin it has formed; also known as insulin resistance and or being unable to synthesis enough insulin. The occurrence has been steadily increasing throughout the world. DM is becoming a fast epidemic in some countries of the world with great number of people affected. This would expect to be double in the next decade due to increase in ageing population. It is also a one of the leading cause of death worldwide [1]. Patients with type 2 DM are more vulnerable to various forms of complications both short- and long-term, which often lead to their death in young age. This tendency of increased morbidity and mortality is seen in patients with type 2DMbecauseofits insidious onset and late recognition, especially in resource-poor developing countries like Africa [2]. In 2014, the International Diabetes Federation estimated that 387 million people around the world had DM, and by 2035 this number is likely to rise to 592 million. Factors such as inactive lifestyle, dietary modifications, ethnicity, and obesity have led to a remarkable increase in the occurrence of DM, particularly in the twenty-first century [3].Diabetes mellitus (DM) is almost certainly one of the oldest diseases known to man. It was first reported in Egyptian manuscript about 3000 years ago [4]. In 1936, the difference between type 1 and type 2 DM was clearly made. Type 2 DM was first described earlier as a factor of metabolic syndrome [5]. Type 2 DM (formerly known as non-insulin dependent DM) is the most common form of DM characterized by hyperglycemia, insulin resistance, and relative insulin deficiency [6]. Type 2 DM results from statement among genetic, environmental and behavioural hazard factors [7]. In type 2 diabetes mellitus (T2DM) the primary defects observed are insulin resistance and abnormal insulin secretion by pancreatic beta-cells. DM is a common metabolic disorder considered by absolute or relative deficiencies in insulin secretion and/or insulin action associated with chronic hyperglycemia and conflict of carbohydrate, lipid and protein metabolism. The thyroid gland is significantly concerned in metabolism of lipid and carbohydrate, role in adipogenesis and thermogenesis, regulation of body weight [8]. Thyroid dysfunction may also interfere in control of diabetes. Hyperthyroidism is characteristically associated with deteriorating glycemic control and amplified insulin requirements. There is primary increased hepatic gluconeogenesis, rapid gastrointestinal glucose absorption, and probably increased insulin resistance. Indeed, thyrotoxicosis may unmask latent diabetes. The most common thyroid disorder is hypothyroidism. The association of thyroid disorder with diabetes is more frequent in diabetics who have deranged metabolic control. Thyroid hormones also influences the glycosylated haemoglobin levels [9]. In practice, there are several implications for patients with both diabetes and hyperthyroidism. First, in hyperthyroid patients, the diagnosis of glucose intolerance needs to be considered cautiously, since the hyperglycemia may improve with treatment of thyrotoxicosis. Second, underlying hyperthyroidism must be considered in diabetic patients with unexplained worsening hyperglycemia. Third, clinician need to anticipate potential deterioration in glycemic control and initiate the treatment accordingly in patients with diabetes and hyperthyroidism to lower the blood glucose level which will result in euthyroidism restoration [10].Although wide-ranging changes in carbohydrate metabolism are seen in hypothyroidism, clinical manifestation of these abnormalities is seldom conspicuous. However, the condensed rate of insulin degradation may inferior the exogenous insulin condition. More importantly, hypothyroidism is accompanied by a variety of abnormalities in plasma lipid metabolism, including elevated triglyceride and low-density lipoprotein (LDL) cholesterol concentrations [11]. Even subclinical hypothyroidism can exacerbate the coexisting dyslipidemia commonly found in type 2 diabetes and further increase the risk of cardiovascular diseases. Lipid abnormalities can be reversed by replacement of sufficient thyroxine in patients with hypothyroidism. Prevalence of thyroid dysfunction is higher in type 2 diabetes patients compared to normal population. Diabetes mellitus and thyroid dysfunction are the most common endocrine diseases seen among the adult population [11] while insulin or thyroid hormones metabolism can result in functional abnormalities of one another. The strong link between diabetes and thyroid diseases encouraged the American Diabetes Association (ADA) to propose that patients with diabetes must be checked periodically for thyroid dysfunction [12]. Thyroid hormones may influence glucose level through a variety of actions on intermediary metabolism. Excess thyroid hormones promote hyperglycaemia by increasing insulin clearance, intestinal glucose absorption, and glycogenolysis and gluconeogenesis. Also, hyperthyroidism is associated with increased hepatic glucose output, reduced insulin action and increased lipolysis [13]. Accordingly, diabetic patients with overt hyperthyroidism may experience poor glycaemic control and indeed hyperthyroidism has been known to induce diabetic ketoacidosis in patients with diabetes [14]. Thyroid disease must be screened every year in diabetic patients to detect asymptomatic thyroid dysfunction [15]. e same time, patients with thyroid dysfunction may require to be tested for the prospect of abnormal glucose metabolism, since extreme thyroid hormones cause increased glucose production in the liver, rapid absorption of glucose through the intestine and increased insulin resistance [16]. There are

many risk factors known to be associated with thyroid dysfunction in the general population, including age, gender, BMI, family history of thyroid disease, smoking, and pregnancy. Incidence of hyperthyroidism and hypothyroidism increases with age, especially beyond 30years, and it has been established that female gender is 10–20 times more likely to have this medical problem than males [17]. Morbidly accounting for 19.5% obese individuals show a high prevalence of overt and subclinical hypothyroidism [18]. Risk factors for thyroid dysfunction among diabetic patients are similar to what have been reported in non-diabetics, although they will vary with the type of thyroid dysfunction, while hypothyroidism among diabetic patients is more prevalent among women [18] and the older population [19].Thus, the present study was intended to explore thyroid dysfunction and associated risk factors among type 2 diabetes mellitus patients in Tamil Nadu.

MATERIAL AND METHODS

A cross-sectional study was carried out during the periodofFebruary2016toJune2017among Type 2 diabetes patients on treatment for 3 years with age group of more than 30 to 50 years . 100 patients were taken for the study attending the outpatient department of Karpaga Vinayaga Institute of Medical Science for regular health checkup who have no known significant medical illness which can affect the outcome of the study.This study was ethically approved by the institutional ethical committee. Age and Body mass index was quantified by bioelectrical impedance analysis. Blood samples for TSH, T4, T3, total cholesterol (TC), triglycerides (TGL), HDL-C, LDL-C, levels along with a written consent were taken from every patient. Fasting Serum sample from cases as well as control group was obtained to determine the following investigations. Thyroid function tests were measured by (Avantor Performance Materials, India) kit using Enzyme linked Immunosorbent assay (ELISA). Normal range of thyroid tests was TSH: 0.39–6.16 (µIU/ml), Free T4: 0.8-2.0(ng/dl) andFT3:1.4-4.2(pg/ml). Patients with TSH levels>6.2 (µIU /ml) with normal FT4 & FT3 values were accepted to have SCH. Total cholesterol (130-250 mg/dl), triglycerides (60-170 mg/dl), HDL – cholesterol (male:35-80mg/dl;female:42-88mg/dl)VLDL (20-40mg/dl), LDL (80-150 mg/dl). Blood sugar fasting (70-110 mg/dl) and post prandial (upto 130 mg/dl) and renal function test such as urea (15-40 mg/dl), creatinine (male: 0.9-1.4 mg/dl; female 0.8-1.2 mg/dl) was investigated by GOD/POD method, enzymatic method respectively. HBA1C (5- 7%) Immunoturbidimetry method was used for investigation. The subjects were studied in terms of their thyroid dysfunction and its risk factors among type 2 diabetes. The study parameter used were: Age (30-50 years), Gender (males and females), Physical activity and exercise wise: low, moderate, high, Socioeconomic condition, Body mass index (BMI), Alcohol intake, Blood pressure.

Exclusion criteria: Type I diabetes mellitus patients, Patients on medications affecting thyroid function, Total and hemi thyroidectomy individuals, Gestational diabetes mellitus, Corticosteroid therapy, Diabetic keto acidosis, Neurodegenerative diseases, Cerebrovascular diseases, Tuberculosis, Cancer.

Statistical Analysis

This study was done to evaluate serum thyroid profile, lipid profile and renal parameters in type 2 diabetes mellitus patients and was done in total number of 100subjectsofwhich50 patients were males and 50 patients were females. The data were analyzed by using standard Mean deviation, student's T test, % graph to compare the levels of various biochemical parameters in age- categorized male and female patients. Univariate analysis was performed to evaluate the gender, age and Thyroid dysfunction with glycemic control. p- value of <0.05 was considered as statistically significant.

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RESULTS

Figure 1: Assessment Of Status Of Diabetes Mellitus In Study Group

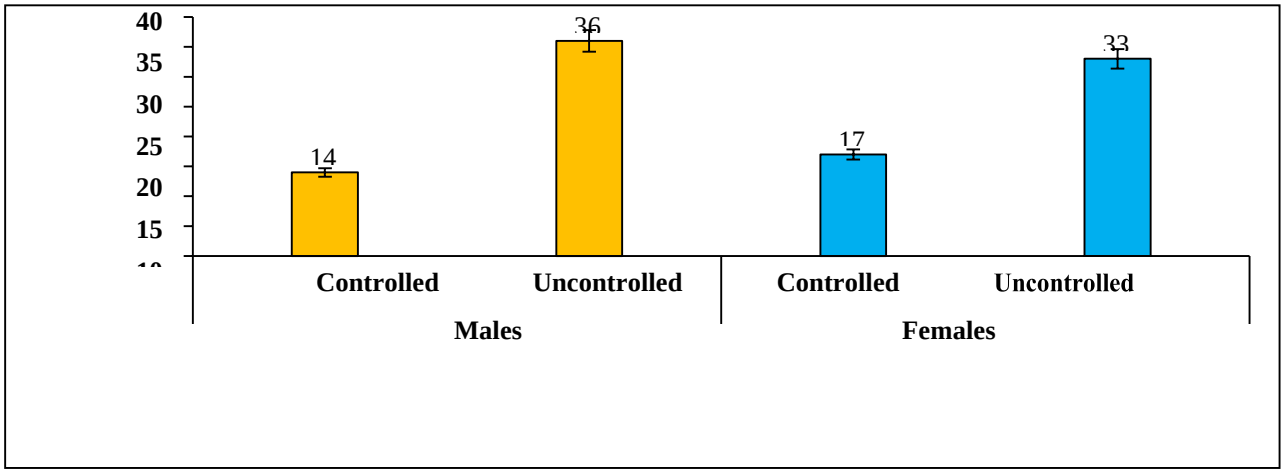

Figure 1 Represents the assessment of status of diabetes in males and females among various age groups. P value <0.05 is considered as statistically significant. Each bar represents controlled and uncontrolled diabetes among male and female through HbA1c levels. First column bar: Males with HbA1c 6.0 – 7.0; Second column bar: Males with HbA1c>7.0; Third column bar: Females with HbA1c6.0–7.0; Fourth column bar: Females with HbA1c >7.0 Cases. Total number of cases: 50 (Males), 50 (Females). Each bar represents the assessment of status of diabetes in males and females among various age groups. P value is<0.05 and it is statistically significant. From this assessment it is clear that uncontrolled diabetes is more in males when compared to females.

Figure 2: Dysfunction In Diabetic Patients Among Various Age Group

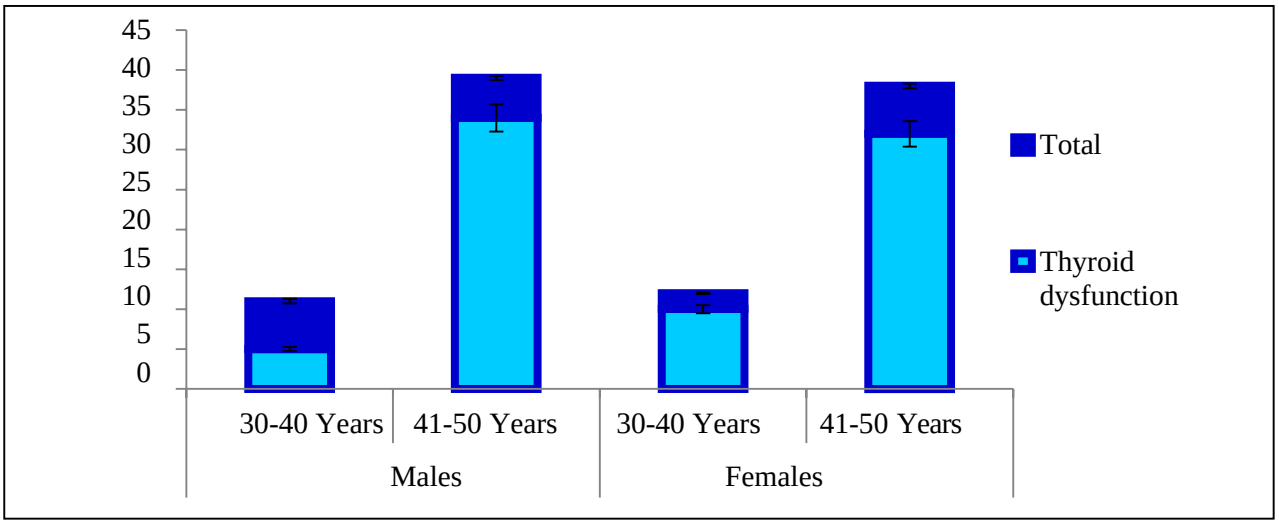

Figure 2 Represents the assessment of thyroid dysfunction in diabetic males and females among various age groups. P value is <0.05 and it is statistically significant. Total number of individuals: 50 (males), 50 (females)**.**Each stacked bar represents thyroid dysfunction in diabetic individual. From this assessment, the number of males with thyroid dysfunction at the age of 30-40 years are less when compared to females in the same age group. P value is <0.05 and is statistically significant. The second stacked bar of this assessment shows that there is no much difference in both genders at the age group of 41-50 years with thyroid dysfunction in diabetic patients. But there is higher incidence of thyroid dysfunction in type 2 DM in the age group of 41-50 years in both genders when compared to age group of 30-40 years.

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Figure 3: Correlation Between Thyroid Dysfunction And Diabetes Based On Hba1c

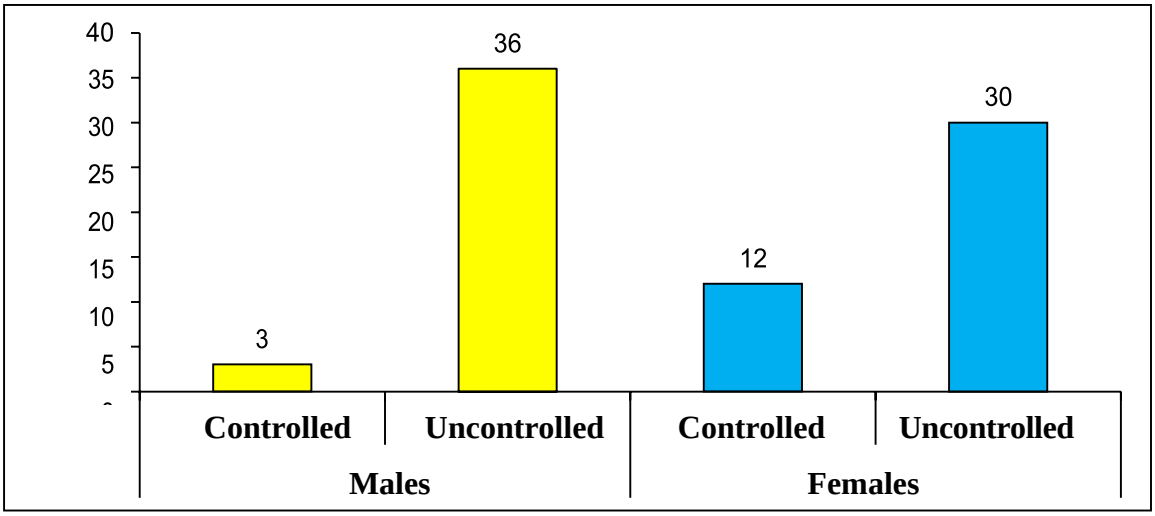

Figure 3 Represents correlation between thyroid dysfunction and diabetes in males and females among various age groups. P value is <0.05 and it is statistically significant. Each bar represents controlled and uncontrolled diabetes among thyroid dysfunction in males and females. First column bar: Males have with thyroid dysfunction among controlled diabetes. Second column bar : Males with thyroid dysfunction among uncontrolled diabetes. Third column bar : Represents Females with thyroid dysfunction among controlled diabetes. Forth column bar : Shows Females with thyroid dysfunction among uncontrolled diabetes .Total number of individuals: 50 (Males), 50 (Females). From this assessment, it is observed that thyroid dysfunction in females is greater even if they have controlled diabetes when compared to males. But thyroid dysfunction in males with uncontrolled diabetes is higher than females with uncontrolled diabetes. There is more incidence of thyroid dysfunction in females even if they have controlled diabetes.. This may be linked with their reproductive age.

Figure 4: Incidence Of Hyperlipidemia (Triglycerides) In Diabetic Patients

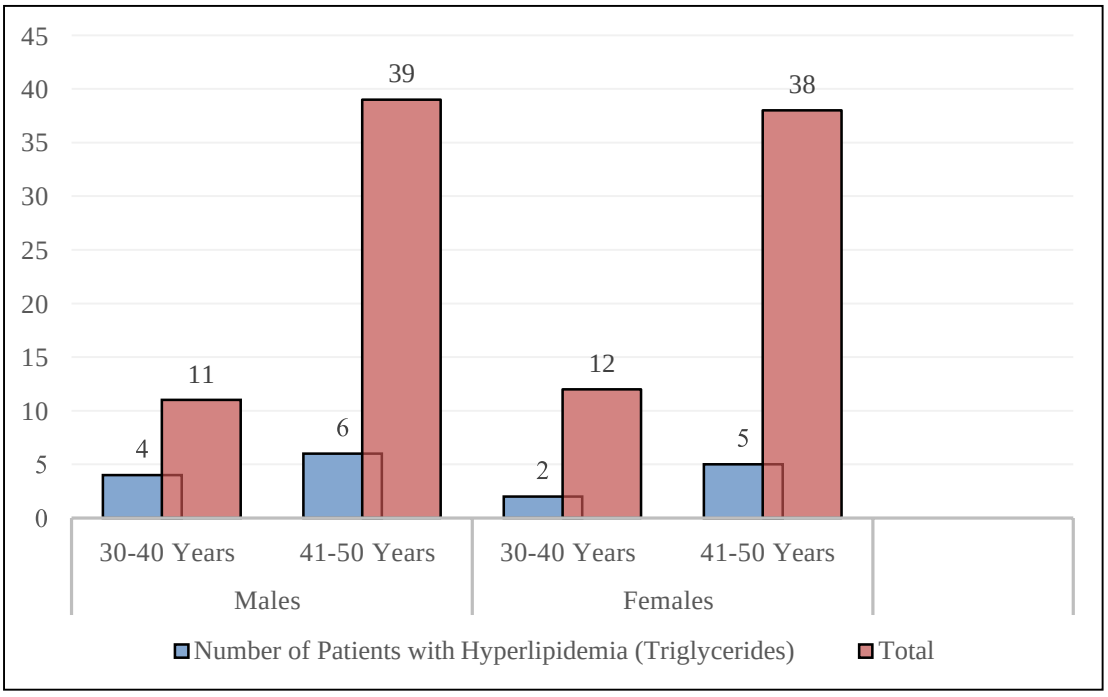

Figure 4 Incidence of hypertriglyceridemia (triglycerides) in diabetic patients. Total number of individuals: 50 (Males), 50 (Females). This stacked bar diagram is a representative of the incidence of hypertriglyceridemia (triglycerides) in both diabetic males and females. P value is <0.05and it is statistically

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significant. Each bar represents incidence of hypertriglyceridemia (triglycerides) in both diabetic males and females. First column bar: Represents 4 Males at the age of 30-40 years are having hypertriglyceridemia (triglycerides). Second column bar: Represents 6 Males at the age of 41-50 years are with hypertriglyceridemia. Third column bar shows 2 Females at the age of 30-40 years having hypertriglyceridemia . Fourth column bar shows 5 Females at the age of 41-50 years are having hypertriglyceridemia . From this assesment it is observed that incidence of hypertriglyceridemia is higher in males when compared to females.

Figure 5: Incidence Of Hyperlipidemia (Total Cholesterol) In Diabetic Individuals

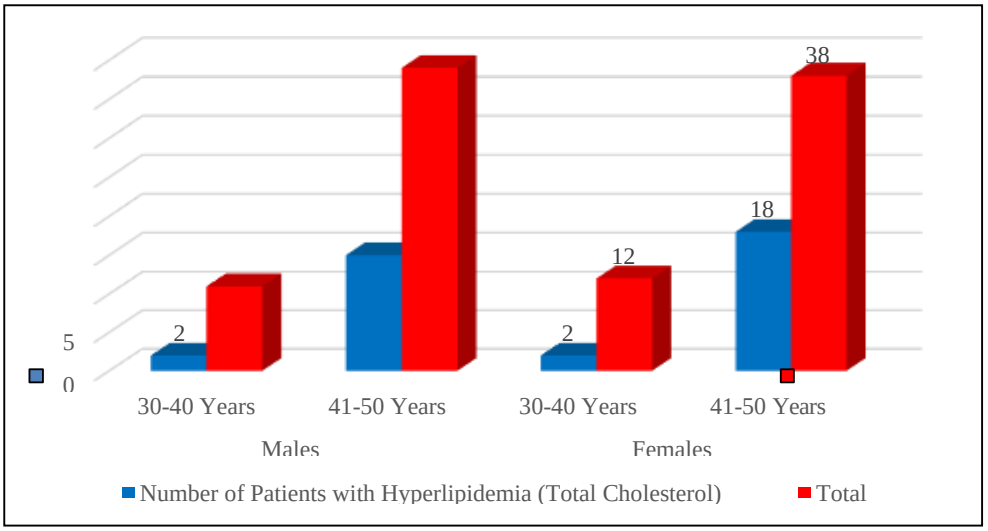

Figure: 5 Incidence of hypercholesterolemia (total cholesterol) in diabetic individuals. Total number of individuals: 50 (Males), 50 (Females). This stacked bar diagram is a representative of the incidence of hypercholesterolemia (total cholesterol) in both diabetic males and females. P value is <0.05 and it is statistically significant. Each bar represents incidence of hypercholesterolemia (total cholesterol) in both diabetic males and females. First column bar: Represents 2 Males at the age of 30-40 years having hypercholesterolemia (total cholesterol). Second column bar represents 15 males at the age of 41-50 years are with hypercholesterolemia Third column bar shows 2 females with hypercholesterolemia . Fourth column bar: Represents 18 females at the age of 41-50 years are with hypercholesterolemia. So it is observed that incidence of hypercholesterolemia is higher in females than males in the age group of 41-50 years

Figure 6: Co-Incidence Of Thyroid Dysfunction With Hyperlipidemia In Diabetic Patients

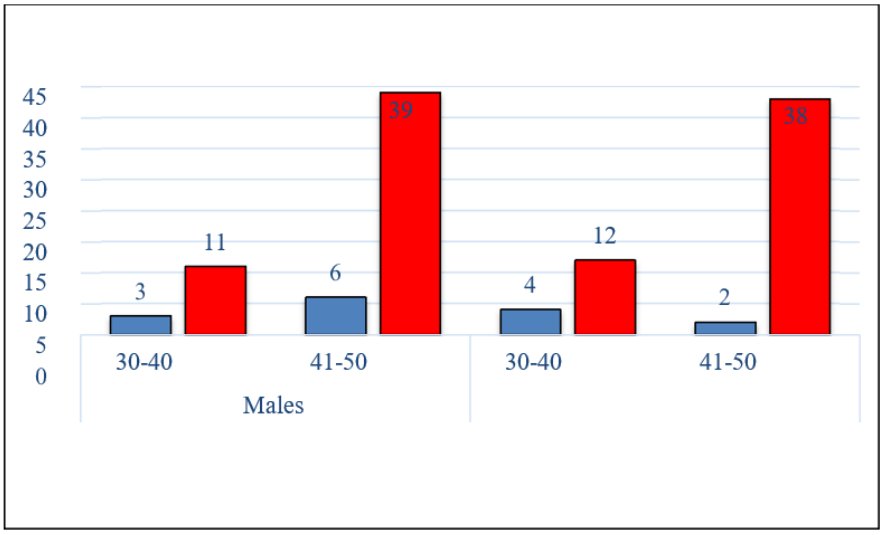

Figure 6 Co-incidence of thyroid dysfunction with hyperlipidemia in diabetic individuals. Total number of individuals: 50 (Males), 50 (Females). This stacked bar diagram is a representative of the co-incidence of thyroid dysfunction with hyperlipidemia in both diabetic males and females. $p<0.05$ is considered as statistically significant. Each bar represents co-incidence of thyroid dysfunction with hyperlipidemia in diabetic males and females. It is observed that the Co-incidence of thyroid dysfunction with hyperlipedemia is higher in male diabetic patients when compared to female diabetics.

DISCUSSION

In our study, we reported a higher prevalence of thyroid dysfunction among both gender of diabetic patients. In a study by Perros et al [20]. the prevalence of thyroid dysfunction was 10.9% in females and 6.9% in males [20]. NHANES III study reported that the prevalence of subclinical hypothyroidism was 3.4% in males and 5.8% in females [21]. In addition, a study in 420 adult females with T2D randomly selected from participants in the community-based Fremantle Diabetes Study showed that the prevalence of subclinical hypothyroidism was8.6% [22]. Finally, are cent study revealed the prevalence of subclinical hypothyroidism was 5.2% in males and 8.4% in females with T2D [23]. Our study results showed that male diabetic patients had poorer glycemic control with higher HbA1clevel when compared to females. The FBS levels were slightly higher in males when compared to females. The levels of TGs were higher in males than females. Total cholesterol was slightly higher in females than males. Also the levels of renal parameters like urea and creatinine were increased in diabetic males when compared to diabetic females since there is poor glycemic control in males. In the present study we also observed that thyroid dysfunction in females is greater even if they had controlled diabetes when compared to males. But thyroid dysfunction in males with uncontrolled diabetes is higher than females with uncontrolled diabetes. There is more incidence of thyroid dysfunction in females even if they had controlled diabetes. This may be linked with their reproductive age. It is observed that the Co-incidence of thyroid dysfunction with hyperlipedemia and renal failure is higher in male diabetic patients when compared to female diabetics. Higher levels of FBS, TG , TC, similar to other studies [24, 25]. The cause of dyslipidemia in type 2 diabetes mellitus may be due to impaired liver apolipoprotein production which in turn regulates the enzymatic activity of lipoprotein lipase and cholesterol ester transport protein [26]. In the present study we found that diabetic patients with thyroid disorders had derangement in lipid profile, with respect to TGL and total cholesterol levels. The existing literature data regarding the association between hyperlipidemia and thyroid dysfunction supports the present study. While dyslipidemia is a reported complication of overt hypothyroidism in diabetic [27, 28] subclinical hypothyroidism does not seem to be associated with dyslipidemia. A study by Chubb et al. did not find any significant relationship between subclinical hypothyroidism and the presence of dyslipidemia. Also, in large studies of subclinical hypothyroidism and coronary heart disease [29, 30]. there was no association with raised serum cholesterol. The levels of HbA1cwere higher in male patients when compared to females. Diabetes confers markedly increased risk of cardiovascular complications among both males and females [31]. However, women with diabetes are more susceptible to increased cardiovascular mortality [32]. They are subject to more adverse changes in coagulation, vascular function and cardiovascular risk factors than diabetic men. Serum TGL increases with poor glycemic control among males unlike females. The results of lipid profile showed that male diabetic patients had higher levels of TGL cholesterol, which is in agreement with earlier reports [33, 34]. This may be attributed to the effects of sex hormones on body fat distribution, leading to differences in altered lipoproteins [35]. Glucose lowering is essential for the prevention of micro vascular complication, and improvement in cholesterol is central to reducing cardiovascular disease in these patients [25]. A significant correlation dyslipidemia (increased TGL) has been observed in type 2 diabetics, suggesting their increased susceptibility to vascular disease [36]. It is likely that the combination of thyroid dysfunction, hyperglycemia, dyslipidemia, Insulin resistance and hypertension as in metabolic syndrome produces an enhanced atherogenic environment within the circulation.

CONCLUSION

In the presence study, the serum levels of FBS, PPBS, HbA1c, Thyroid profile, urea, Creatinine and lipid profile were evaluated in type 2 Diabetes mellitus patients of both gender in the age group of 30-50 years. Our study results showed poor glycemic control with higher HbA1c levels in male diabetic patients when compared to females. Assessment of Thyroid profile showed thyroid dysfunction is greater in females even if they had controlled diabetes when compared to males. Thyroid dysfunction is higher in males with uncontrolled diabetes when compared to females with uncontrolled diabetes. It seems that more incidence of thyroid dysfunction in females even if they had controlled diabetes. This may be associated with their

reproductive age. The present study showed that the prevalence of thyroid dysfunction among Indian diabetic patients attending an outpatient clinic was 12.3%. The levels of urea and creatinine were raised in diabetic males when compared to diabetic females since there is poor glycemic control in males indicating higher incidence of renal failure in diabetic males. The levels of TGL were higher in diabetic males when compared to females. It is observed that the Co-incidence of thyroid dysfunction with hyperlipidemia and renal failure is higher in male uncontrolled diabetic patients when compared to female diabetics. Hence, it is concluded that thyroid dysfunction is positively associated with hyperlipidemia and renal dysfunction in type 2 diabetes mellitus. So the estimation of serum thyroid profile , lipid profile and renal parameters is highly beneficial in type 2 diabetes mellitus patients to assess the cardiovascular and renal complications. treatment and follow up of thyroid dysfunction with hyperlipidemia may prevent or decrease the development of cardiovascular and renal complications in type 2 diabetes mellitus. . Further research is needed to elucidate the exact molecular mechanism behind the link between hyperlipidemia and thyroid dysfunction in type2 DM and the life style modification also to be assessed.

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