



# Metabolic consequences of hypothyroidism: impact on glycemic regulation, liver health and lipid metabolism

Shrikant Sharma<sup>1#</sup>, Don Mathew<sup>2#\*</sup>, Ashish Kumar Sharma<sup>3</sup>, Vasudev Sankhla<sup>1</sup>, Suraj Pal Singh<sup>1</sup>, Neelam Bhatia<sup>4</sup>, Disha Sahi<sup>5</sup>

<sup>1</sup>Ph.D. Research Scholar, Department of Biochemistry, Faculty of Medicine, Pacific Medical College and Hospital, Pacific Medical University (PMU) Udaipur, Rajasthan, IND

<sup>2</sup>Assistant Professor, Department of Biochemistry, Faculty of Medicine, Pacific Medical College and Hospital, Pacific Medical University (PMU) Udaipur, Rajasthan, IND

<sup>3</sup>Assistant Professor, Department of Biochemistry, Madhav Prasad Tripathi Medical College, Siddharthnagar, U.P., India.

<sup>4</sup>Resident, Department of Psychiatry, Faculty of Medicine, S. N. Medical College Jodhpur, Rajasthan, IND

<sup>5</sup>Intern, Department of Biochemistry, Faculty of Medicine, Pacific Medical College and Hospital, Pacific Medical University (PMU) Udaipur, Rajasthan, IND

*#These authors have contributed equally to the work and share first authorship*

*\*Corresponding Author: Don Mathew, mathewdon2@gmail.com*

## ABSTRACT:

**Background:** Patients with diabetes have an increased risk of thyroid disease. The appearance of thyroid dysfunction in people with diabetes is greater than in the general population, while almost a third of people with type 1 diabetes (T1DM) ultimately develop thyroid dysfunction. Thyroid dysfunction can impair liver function, liver disease impairs thyroid hormone metabolism, and many systemic diseases affect both organs.

**Method:** The study involved 300 participants, 150 Diabetes Mellitus patients and 150 healthy controls. We further evaluated Blood sugar levels, and serum lipid profiles levels using Mindray BS240 analyzer and Triiodothyronine [T3], thyroxine [T4] and thyroid stimulating hormone [TSH] were measured by Chemiluminescence immunoassay.

**Result:** Diabetic patients had deranged levels of T3 (OR 2.031, P Value 0.001\*), T4 (OR 1.734, P Value 0.001\*), and TSH (OR 3.147, P Value 0.001\*) and higher levels of FBS, PPBS, RBS, total cholesterol (OR 3.120, P Value 0.001\*), triglycerides (OR 1.592, P Value 0.001\*), HDL (OR 2.173, P Value 0.001\*), LDL (OR 2.110, P Value 0.001\*), and VLDL (OR 2.194, P Value 0.001\*) compared to healthy controls.

**Conclusion:** This study shows that diabetic hormones have a significant effect on thyroid function in patients with diabetes and hypothyroidism. This is important for diabetic patients because thyroid functions can be adjusted by insulin resistance and glucagon level changes.

**Keyword:** Hypothyroidism, diabetes mellitus, LFT.



## **INTRODUCTION:**

The two most prevalent endocrine illnesses that have a significant impact on metabolism are diabetes (DM) and thyroid issues [1,2]. These disorders commonly coexist because of the close metabolic links between the thyroid and pancreas. [3,4]. Insulin sensitivity, basal metabolic rate, and glucose metabolism are all regulated by the thyroid hormones triiodothyronine (T3) and thyroxine (T4).[4,5,6]. Any imbalance in thyroid hormones, such as hypothyroidism or hyperthyroidism, can significantly affect glucose homeostasis and, consequently, diabetics' ability to control their blood sugar levels.[7,8]. Thyroid hormone imbalance alters various physiological processes that are fundamental to glucose metabolism[3,5,6]. Hyperthyroidism is associated with increased gluconeogenesis, intestinal glucose absorption, and insulin resistance, all of which can make diabetics' hyperglycemia worse[9,10]. Still, by decreasing peripheral glucose utilize and impairing insulin secretion, hypothyroidism may be a contributor to incidents of hypoglycemia or inappropriate glycemic control. [11,12]. In diabetic patients, where maintaining ideal glycemic control is essential to avoiding long-term complications like neuropathy, nephropathy, and cardiovascular diseases, these effects are especially worrisome[13,14,15]. The postprandial blood glucose response to carbohydrate intake is measured by the glycemic index (GI), which is an essential metric for understanding dietary control in diabetes[16,17,18]. Thyroid disease may further alter this response by altering glucose metabolism at the cellular and systemic levels [3,4,9]. Previous study has clearly demonstrated that individuals with primary cirrhosis of the liver or autoimmune chronic active hepatitis (CAH) have an even higher prevalence of antithyroglobulin antibodies (ATA) and a higher incidence of thyroid dysfunction than would be predicted Antibody against microorganisms (AMA). The previous study did not investigate the mechanisms by which liver disease affects thyroid hormone metabolism and function.

The previous study did not explore the relationship between liver disease and thyroid dysfunction in more detail[42]. The liver synthesizes a number of plasma proteins that bind the lipid-soluble thyroid hormones, thereby providing a large and rapidly exchangeable pool of circulating hormone [43].

## **AIM/OBJECTIVE OF STUDY:**

The aim of this study is to investigate the effects of hypothyroidism on blood glucose levels, lipid metabolism, and liver function and the objectives are



- 1.To elucidate the mechanisms by thyroid hormone metabolism affect liver disease and function.
- 2.To evaluate the impact of thyroid hormone levels and thyroid function tests on lipid metabolism.

## **MATERIALS AND METHODS:**

This cross-sectional observational study, conducted at the Department of Biochemistry, Pacific Medical College and its associated group of hospital, Pacific Medical University, Udaipur, Rajasthan, India, aimed to examine the interplay between Type 2 diabetes mellitus, thyroid abnormalities, and LFT.

Diagnostic criteria for type 2 diabetes were American Diabetes Association criteria: fasting plasma glucose level of 110 mg/dL, random plasma glucose level of 200 mg/dL, or taking hypoglycemic drugs or using insulin, and no symptoms of ketosis in the past.

**Sample Size:** Sample size was calculated on the basis of this formula  $n = 4pq/e^2$ . The minimum required sample size is 200 for this study but considering the complexity of the study we recruited 300 participants. Out of 300 participants, 150 were healthy individuals and 150 were T2DM cases.

## **Inclusion Criteria:**

1. Age: Patients aged 30-70 years.
2. Diagnosis: Patients with a confirmed diagnosis of Type 2 Diabetes Mellitus (T2DM).
3. Glycemic Control: Patients with HbA1c levels  $\geq 6.5\%$  and  $\leq 12\%$ .
4. Thyroid Function: Patients with abnormal thyroid function (hypothyroidism).
5. Willingness to Participate: Patients willing to provide informed consent and participate in the study.

## **Exclusion criteria:**

1. Type 1 Diabetes Mellitus: Patients with Type 1 Diabetes Mellitus.
2. Pregnancy and Lactation: Pregnant or lactating women.
3. Severe Illness: Patients with severe illness, such as cancer, liver disease, or kidney disease.
4. Thyroid Cancer: Patients with thyroid cancer.
5. Medications Affecting Thyroid Function: Patients taking medications that affect thyroid function, such as amiodarone or lithium.



6. Previous Thyroid Surgery or Radioactive Iodine Treatment: Patients who have undergone thyroid surgery or radioactive iodine treatment.

7. Inability to Provide Informed Consent: Patients unable to provide informed consent due to cognitive impairment or other reasons.

### **Method of Analysis:**

Detailed history, including duration of diabetes, hypothyroidism, lipid profile details and current medications, was collected. Physical examination included weight, height, and body mass index (BMI) measurements. Thyroid function tests, including FT4, FT3, T3, T4, and TSH, as well as other biochemical analyses, including FPG, HbA1C, and lipid profile, were performed on venous blood samples. The Chemiluminescence Assay method was used to determine T3 (normal range: 0.60–1.78 ng/ml), T4 (normal range: 5.2-12.45 µg/dl), and TSH (normal range: 0.3-5.3 µIU/ml). A fully-automated clinical chemistry analyzer was used to determine the following parameters: FPG (normal range 70-110 mg/dl), HbA1c (normal range 4.2-6.2%), serum cholesterol (normal range 150-200 mg/dl), serum triglycerides (normal range 100-150 mg/dl), serum HDL (normal range 35-48 mg/dl), serum LDL (normal range <130), and serum VLDL (normal range 5-35 mg/dl).

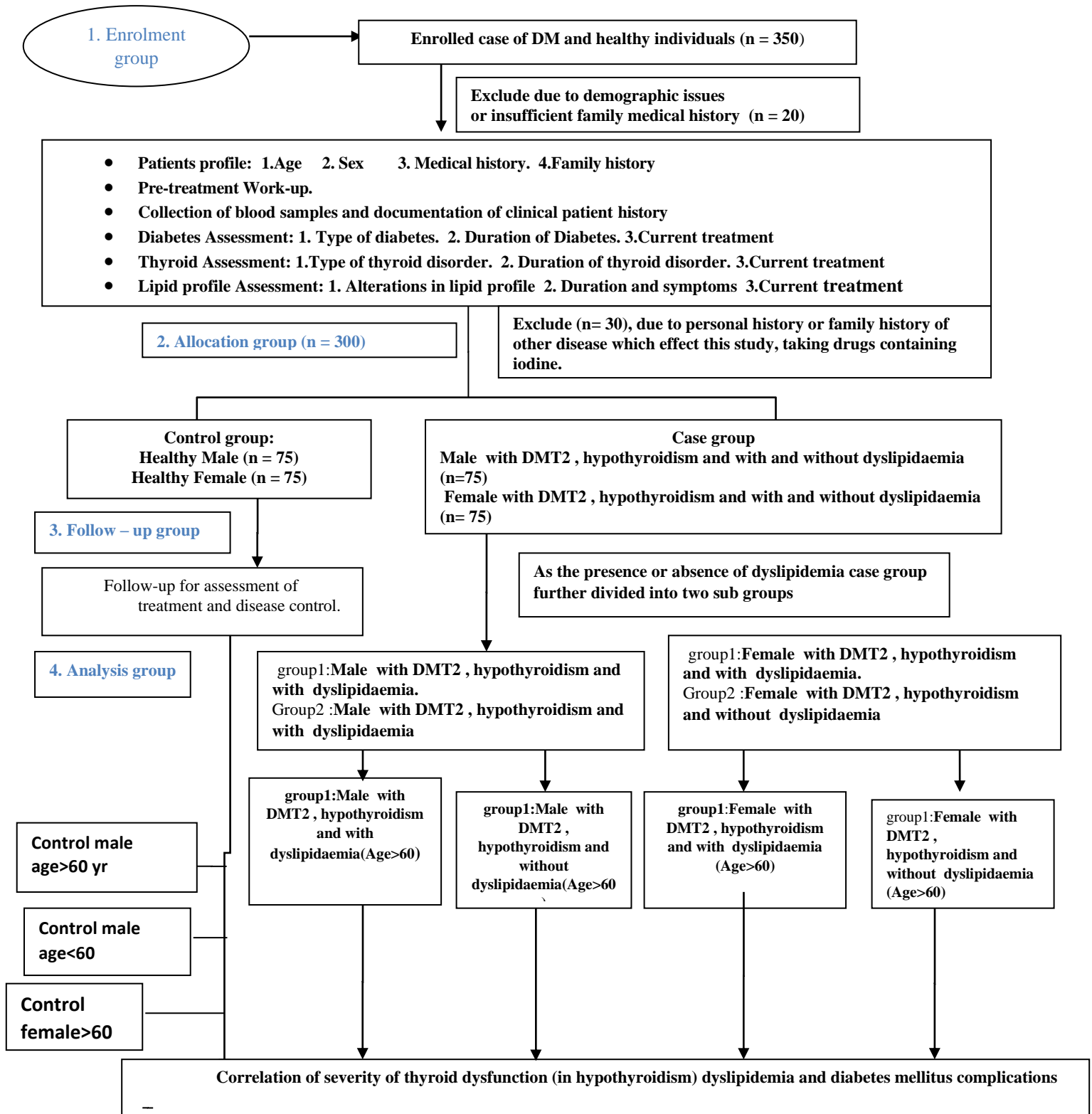
### **Statistical Analysis:**

The statistical analysis was performed by using SPSS version 23. Continuous variables were expressed as mean  $\pm$  standard deviation. The independent t-test was used to compare the means among the variables. Further linear regression was used to estimate the Odds ratio and 95% confidence interval of the parameters. A p-value <0.05 was considered statistically significant.

### **Study Outline:**



**FIGURE No1:** The flowchart of study of Type 2 Diabetics Mellitus ,Hypothyroidism and Dyslipidmia in case and control groups:





**Observation and Results:** This study involved 300 participants, comprising 150 healthy controls (75 males, 75 females) and 150 diabetic patients with thyroid issues (75 males, 75 females) (Table 1). In control group the age range and mean age of male subjects is 30 -70 years and  $39.19 \pm 9.95$  while the age range and mean age for female subjects is 30 -70 years and  $38.17 \pm 10.21$  years, respectively. The control group comprised participants of both males and females with an age range of 30 - 70 years and a mean age of  $38.68 \pm 10.02$  years (Table 1).

**Table 1. Gender and gender distribution of the selected Case and Control.**

Group	Gender	No. of patients	Age	
			Range	Mean $\pm$ SD
Control	Male	75	30-70	$39.19 \pm 9.95$
	Female	75	30-70	$38.17 \pm 10.21$
	Total	150	30-70	$38.68 \pm 10.02$
Case	Male	75	30-70	$56.18 \pm 10.71$
	Female	75	30-70	$53.24 \pm 9.95$
	Total	150	30-70	$52.74 \pm 10.73$

**Table 2. Glycemic parameters, serum lipid profile and serum thyroid profile in case and control group.**

S.No	Parameters	Mean $\pm$ SD Control	Mean $\pm$ SD Case	OR	P-value
1	T3 (ng/ml)	$1.34 \pm 0.34$	$0.61 \pm 0.3$	2.031	0.001 (**)
2	T4 (ug/dl)	$8.5 \pm 1.76$	$4.65 \pm 1.12$	1.734	0.001 (**)
3	TSH (uIU/L)	$2.8 \pm 1.12$	$12.5 \pm 2.46$	3.147	0.001 (**)
4	T. CHO	$170 \pm 32.90$	$289.1 \pm 42.55$	3.120	0.001 (**)
5	TG	$86.6 \pm 18.1$	$205.1 \pm 46$	1.592	0.001 (**)
6	HDL	$50.2 \pm 5.9$	$28.7 \pm 4.08$	2.173	0.001 (**)
7	LDL	$77.65 \pm 13.61$	$140 \pm 24.87$	2.110	0.001 (**)



8	VLDL	17.33 ± 6.8	48.1 ± 13.8	2.194	0.001(**)
9	Creatinine	0.74 ± 0.15	1.05 ± 0.25	1.00	0.0006(**)
10	UREA	29.63 ± 5.9	33.12 ± 8.1	0.792	0.004(**)
11	UA	5.13 ± 1.5	6.3 ± 2.02	1.392	0.001(**)
12	T. Bilrubin	0.69 ± 0.12	1.4 ± 0.38	0.129	= 0.18
13	Conjugated bilrubin	0.16 ± 0.08	0.21 ± 0.1	0.650	0.0073(*)
14	Unconjugated Bilrubin	0.46 ± 0.07	0.65 ± 0.9	0.192	0.001(**)
15	SGPT	31.92 ± 6.9	35.95 ± 8.4	0.176	0.34
16	SGOT	28.97 ± 6.37	33.12 ± 7.3	0.129	0.12
17	ALP	93.76 ± 14	96.76 ± 16.9	0.212	0.52
18	TP	7.32 ± 0.69	7.21 ± 0.71	0.229	0.24
19	Albumin	4.5 ± 0.60	4.32 ± 0.59	0.271	0.029
20	Globulin	2.7 ± 0.46	2.85 ± 0.53	0.117	0.36

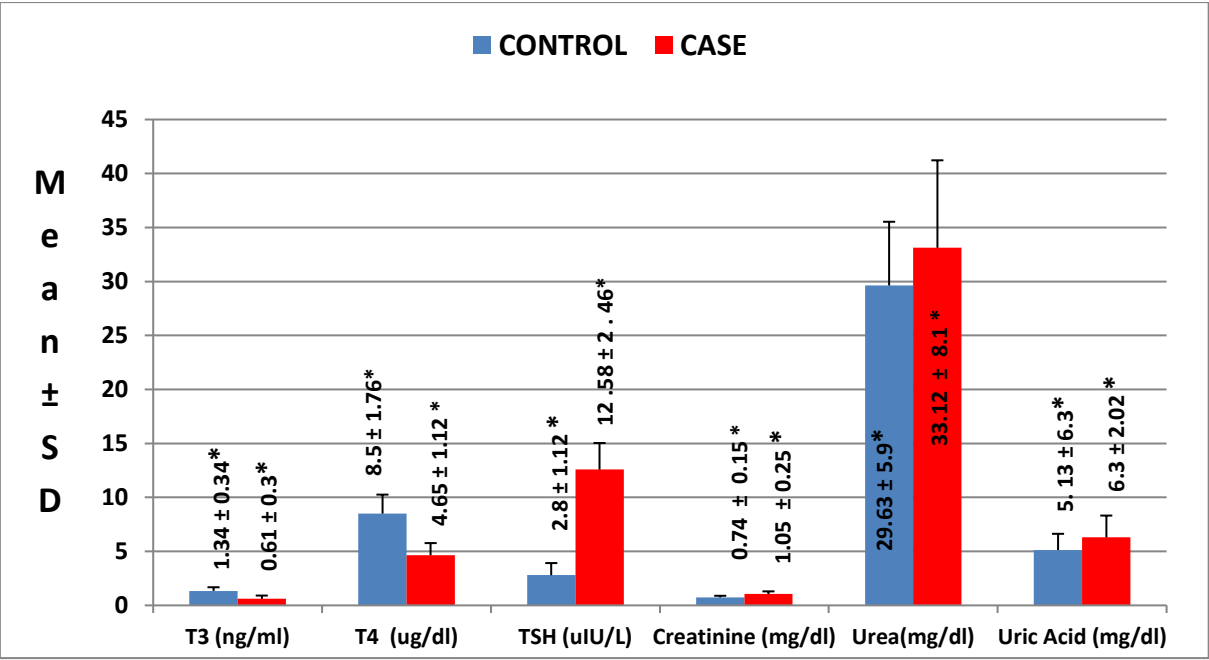


Figure 2 (A): Thyroid profile and RFT in case and control group







Levels of T3 and T4 were significantly decrease in patients with T2DM, T3 (0.61) ng/ml, T4 (4.65 ug/dl) and TSH (12.58)  $\mu$ IU/L, significantly increase compared to control group with the significant p value ( $P < 0.001$ ) and OR (2.031).

Comparison of control group with Case group, results of serum lipid profile showed that the means values for TC, TG, HDL-C, LDL-C and VLDL-C in case group were  $289.1 \pm 42.55$  mg/dl,  $205 \pm 46.8$  mg/dl,  $28.7 \pm 5.9$ mg/dl,  $140 \pm 24.87$  mg/dl and  $48.1 \pm 23.8$  mg/dl respectively. The means values for TC, TG, HDL-C, LDL-C and VLDL-C in control group were  $170 \pm 32.9$  mg/dl,  $86.6 \pm 18.1$  mg/dl,  $50.2 \pm 5.9$  mg/dl,  $77.65 \pm 33.61$  mg/dl and  $17.33 \pm 6.8$  respectively. Results showed that diabetic case have significantly higher ( $P < 0.01$ ) TC, TG and LDL-C as compared to control.

Comparison between hypothyroid diabetic subjects to healthy subject show a statistically significant decrease in HDL-C levels and an increase in serum total cholesterol, triglycerides, LDL-C, and VLDL-C levels were noted ( $p < 0.0001$ ).

**Table 3: Gender wise comparison of thyroid profile, lipid profile and renal function test in Control and Case**

S . N	Parameters	Mean $\pm$ SD Healthy male	Mean $\pm$ SD Healthy female	Mean $\pm$ SD Diabetic male	Mean $\pm$ SD Diabetic Female	OR	P-value
1	T3 (ng/ml)	$1.32 \pm 0.21$	$1.22 \pm 0.28$	$0.56 \pm 0.9$	$0.49 \pm 0.5$	2.19	0.001(**)
2	T4 (ug/dl)	$8.2 \pm 0.14$	$7.6 \pm 1.5$	$4.12 \pm 0.31$	$3.1 \pm 0.29$	1.734	0.001(**)
3	TSH (uIU/L)	$2.68 \pm 1.2$	$3.0 \pm 0.9$	$12.1 \pm 4.37$	$13.68 \pm 5.74$	3.147	0.001(**)
4	T. CHO	$155.5 \pm 31.92$	$134.7 \pm 30.1$	$228.7 \pm 48$	$269.2 \pm 49$	3.120	0.001(**)



5	TG	83.1 ± 19	88 ± 14	238 ± 45	261 ± 48	1.592	0.001(**)
6	HDL	49 ± 8.7	53.1 ± 4.9	26.3 ± 4.9	22 ± 4.08	2.173	0.001(**)
7	LDL	63 ± 18	66 ± 19	178.1 ± 22	241 ± 28	2.110	0.001(**)
8	VLDL	22.1 ± 6.6	25.1 ± 5.1	41.9 ± 21.4	61.85 ± 19.2	2.194	0.001(**)
9	Creatinine	0.74 ± 0.16	0.72 ± 0.1	1.9 ± 0.25	1.21 ± 0.40	1.00	0.048(**)
10	UREA	29.48 ± 6.16	31.1 ± 10.4	39.63 ± 12	35 ± 14.64	0.792	0.29
11	UA	3.6 ± 1.8	4.1 ± 1.3	7.2 ± 2.9	5.91 ± 1.9	1.392	0.35
12	T. Bilrubin	0.62 ± 0.27	0.69 ± 0.32	0.76 ± 0.35	1.9 ± 0.21	0.129	0.39
13	Conjugated Bilrubin	0.13 ± 0.12	0.26 ± 0.7	0.36 ± 0.06	0.82 ± 0.31	0.650	0.21
14	Unconjugated Bilrubin	0.42 ± 0.2	0.46 ± 0.24	0.60 ± 0.31	0.51 ± 1.1	0.192	0.69
15	SGPT	28.5 ± 12.7	26.1 ± 10.8	29.75 ± 28	31.6 ± 8.2	0.176	0.56
16	SGOT	26.1 ± 13.1	28 ± 11.37	35.5 ± 11.67	22.1 ± 9.25	0.129	0.67
17	ALP	94.1 ± 12	93.7 ± 24	91 ± 22	102.8 ± 27	0.212	0.43
1	TP	6.31 ± 0.61	6.5 ± 0.69	9.1 ± 0.6	8.1 ± 0.6	0.229	0.14



8							
1 9	Albumin	5.5 ± 0.43	5.1 ± 0.63	4.1 ± 0.53	4.9 ± 0.53	0.271	0.70
2 0	Globulin	2.1 ± 0.41	2.7 ± 0.46	2.3 ± 0.55	2.1 ± 0.57	0.117	0.27

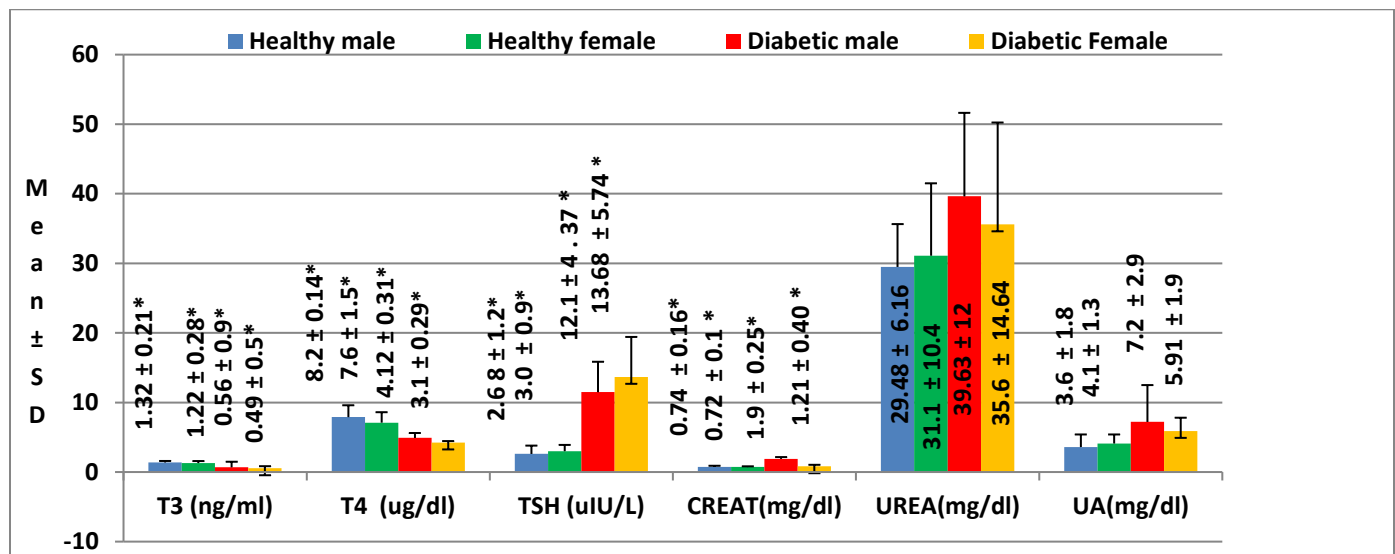


Figure 3:(A) Thyroid profile and RFT in case and control group.

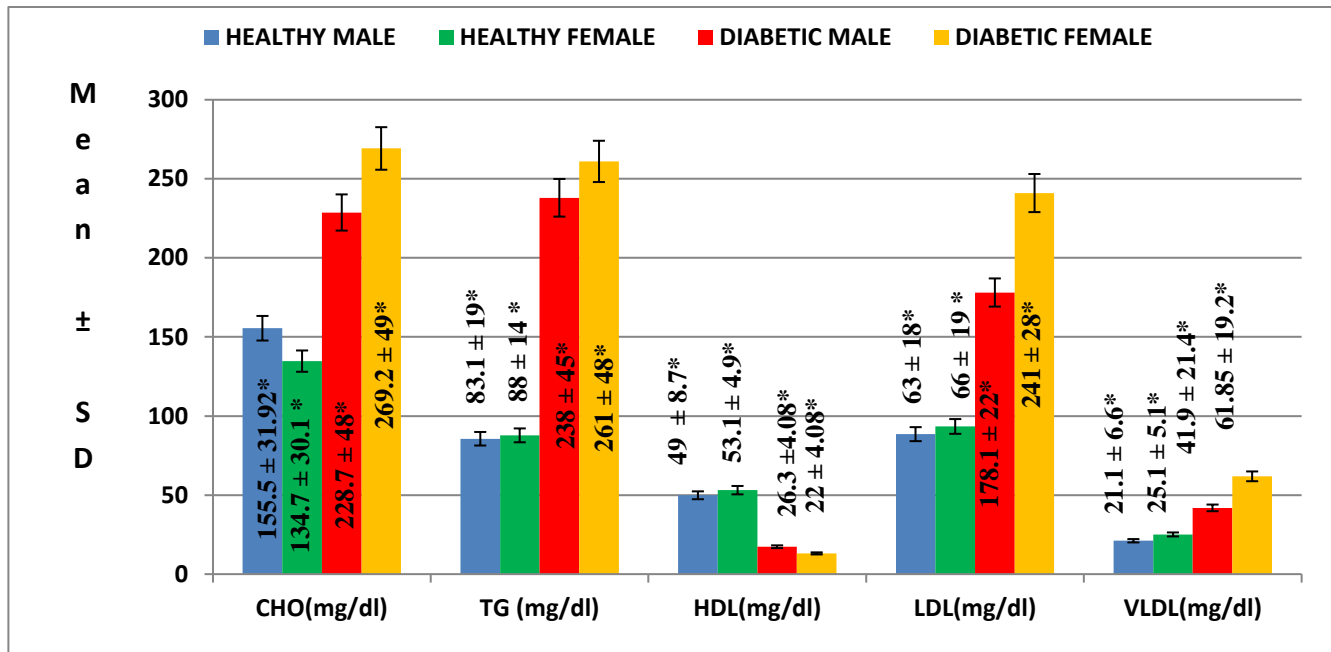


Figure 3 (B) Lipid profile in case and control group.

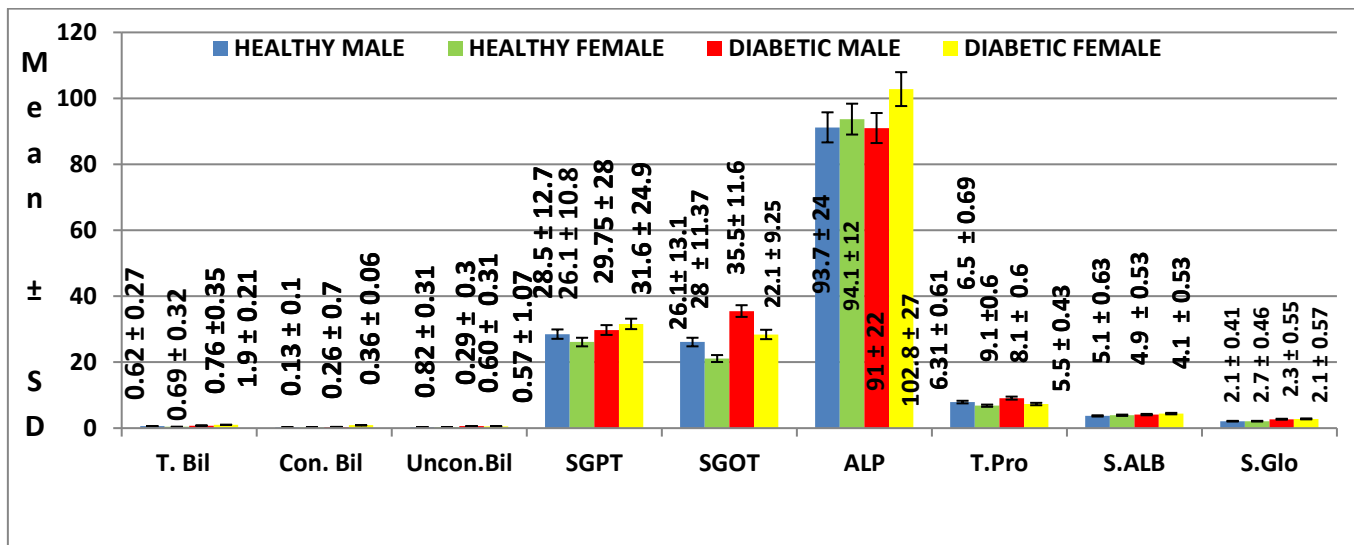


Figure 3 (C): LFT in case and control group



### Figure 3 : Gender wise comparison of thyroid profile, lipid profile and renal function test in Control and Case group

A gender-wise comparison between the control and case groups revealed that hypothyroidism was more prevalent in the study group, particularly among diabetic females. Notably, diabetic females exhibited a significant decrease in T3 levels, with a mean value of  $0.68 \pm 0.8$ , accompanied by decreased T4 levels and elevated TSH values ( $P < 0.001^*$ ). Furthermore, diabetic females showed a highly significant increase in serum total cholesterol, triglycerides, LDL, and VLDL levels, along with a decrease in HDL cholesterol levels. These findings suggest that diabetic females are more prone to hypothyroidism and dyslipidemia compared to other groups.

**Table 4: Comparison of healthy control and case according to age**

S.N 0	Parameters	Mean $\pm$ SD Control < 60Yr	Mean $\pm$ SD Control > 60Yr	Mean $\pm$ SD Diabetic case < 60Yr	Mean $\pm$ SD Diabetic Case > 60 Yr	OR	P-value
1	T3	$1.72 \pm 0.21$	$1.70 \pm 0.28$	$0.42 \pm 0.9$	$0.03 \pm 0.5$	7.0	0.001(**)
2	T4	$9.2 \pm 0.14$	$9.3 \pm 1.5$	$2.12 \pm 0.31$	$1.1 \pm 0.29$	1.734	0.001(**)
3	TSH	$2.2 \pm 1.2$	$2.5 \pm 0.9$	$52.1 \pm 22.4$	$88.1 \pm 19.2$	3.147	0.001(**)
4	T. CHO	$138.1 \pm 46$	$152 \pm 31$	$180 \pm 41$	$203.24 \pm 49$	3.120	0.001(**)
5	TG	$83.1 \pm 19$	$88 \pm 35$	$124.46 \pm 65$	$156.38 \pm 75$	1.592	0.001(**)
6	HDL	$52 \pm 8.7$	$46 \pm 6.2$	$28.1 \pm 53$	$15 \pm 1.5$	2.173	0.001(**)
7	LDL	$63 \pm 38$	$66.5 \pm 32$	$105 \pm 38$	$132 \pm 37$	2.110	0.001(**)
8	VLDL	$33.1 \pm 23.5$	$52.1 \pm 7$	$38.1 \pm 19.7$	$44.3 \pm 25.2$	2.194	0.001(**)



9	Creatinine	0.71 ± 0.12	0.75 ± 0.10	0.89 ± 0.65	1.21 ± 0.5	1.00	0.048(**)
10	UREA	29.48 ± 6.16	31.1 ± 10.4	29.63 ± 22	35.60 ± 28.64	0.792	0.29
11	UA	3.6 ± 1.8	4.1 ± 1.3	7.2 ± 5.3	5.91 ± 11.9	1.392	0.35
12	T. BILRUBI N	0.62 ± 0.27	0.69 ± 0.32	0.76 ± 0.35	1.9 ± 0.21	0.129	0.31
13	Conjugate d Bilrubin	0.13 ± 0.12	0.16 ± 0.08	0.36 ± 0.06	0.82± 0.31	0.650	0.24
14	Unconjuga ted Bilrubin	0.42 ± 0.21	0.46 ± 0.24	0.60 ± 0.31	0.51± 1.1	0.192	0.69
15	SGPT	35.1 ± 22.1	31.92 ± 26.9	29.75 ± 28	17.5± 8.2	0.176	0.032
16	SGOT	31.1 ± 18.2	28.97 ± 16.37	35.5 ± 31	22.1± 10.2	0.129	0.67
17	ALP	94.1± 12	93.76 ± 34	91 ± 39	102.8 ± 46	0.212	0.43
18	TP	6.31 ± 0.61	6.5 ± 0.69	9.1 ± 0.60	8.1 ± 0.6	0.229	0.14
19	Albumin	5.5± 0.43	5.1± 0.63	4.7 ± 0.53	4.9 ± 0.53	0.271	0.81
20	Globulin	2.1± 0.41	2.7± 0.46	2.3 ± 0.55	2.1 ± 0.57	0.117	0.27

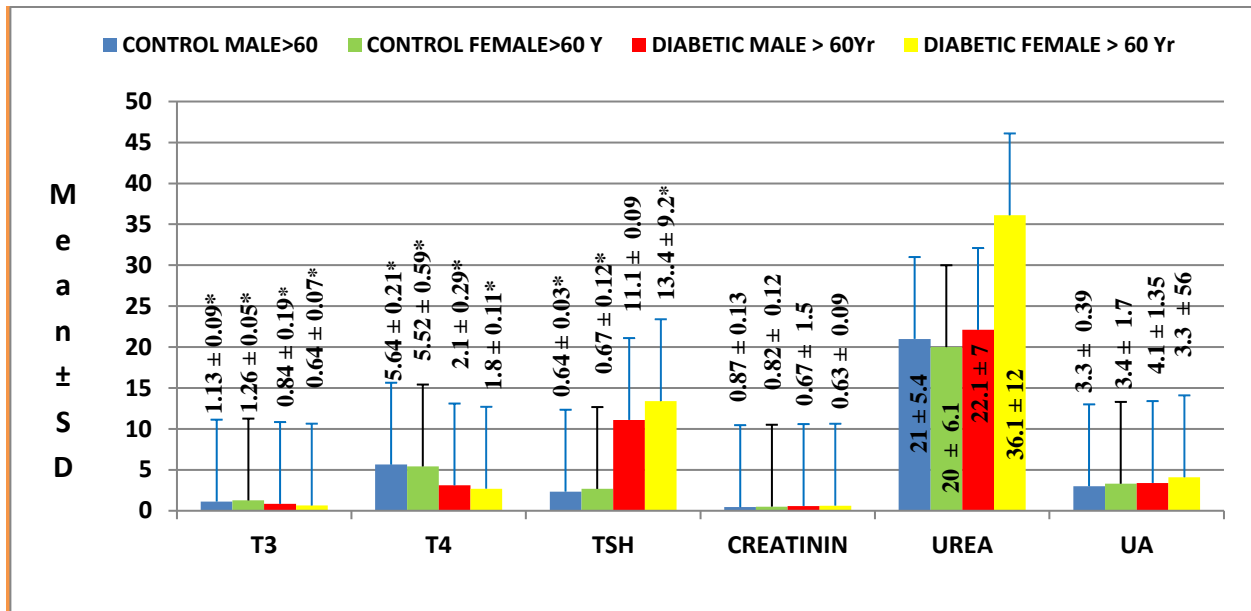


Figure 4(A): Thyroid profile and RFT in control and case group.

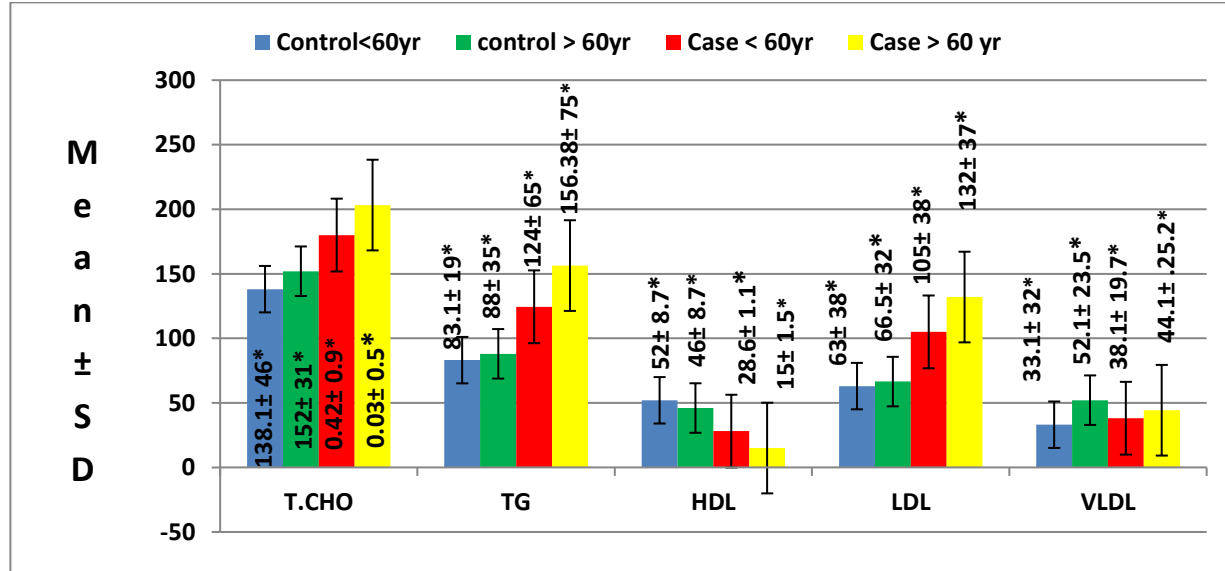


Figure 4 (B): Lipid profile in control and case group.



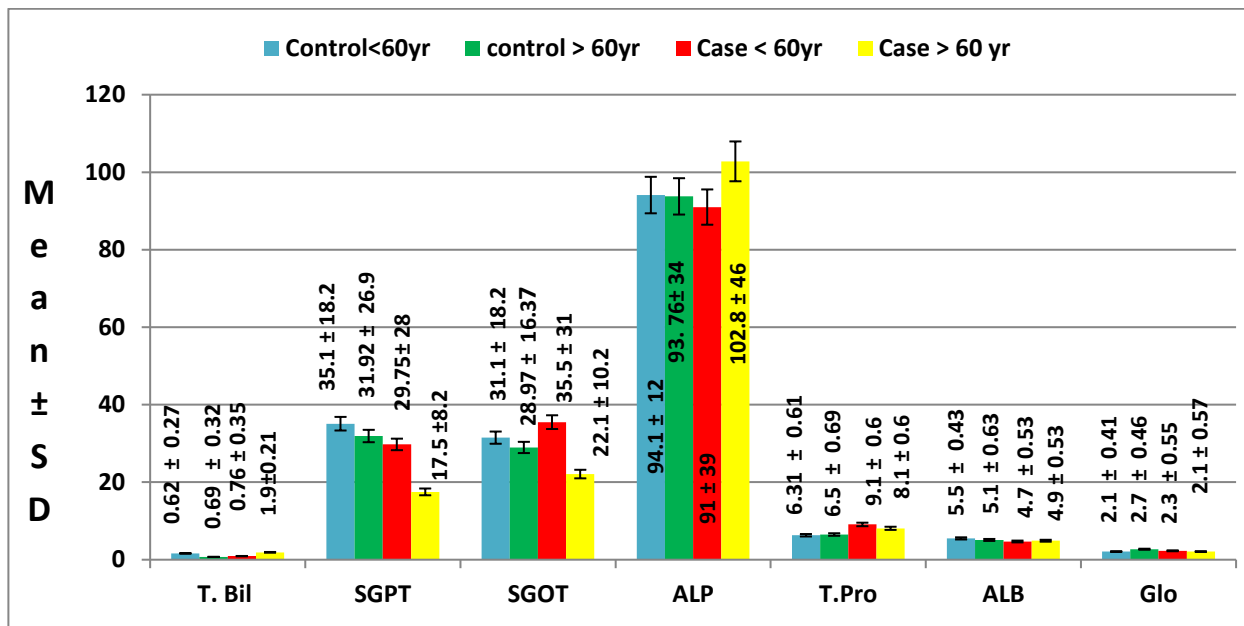


Figure 4 (C): LFT Panel in control and case group.

Figure 4: Comparison of Thyroid profile, RFT (A) and lipid profile (B) and LFT Panel in control and case group.

In the age group above 60 years, T3 and T4 levels were significantly decreased ( $p < 0.01$ ), while TSH levels were significantly increased ( $p < 0.01$ ). Additionally, lipid profiles were significantly high in the diabetic group especially in women. In LFT panel slightly high value of ALP found in case group. These findings suggest that older adults, particularly females, are more susceptible to thyroid dysfunction and lipid abnormalities. T3, T4, TSH and lipid profile significantly deranged in diabetic group. (Table 3)



**Table 5: Comparison of control and case according to gender**

Parameters	Mean $\pm$ SD Control male>60yr	Mean $\pm$ SD Control female >60yr	Mean $\pm$ SD Diabetic male> 60yr	Mean $\pm$ SD Diabetic female >60 yr	OR	P-value
T3 (ng/ml)	1.13 $\pm$ 0.3	1.26 $\pm$ 0.27	0.31 $\pm$ 0.9	0.25 $\pm$ 0.3	1.14	0.001(**)
T4 (ug/dl)	5.64 $\pm$ 1.50	5.52 $\pm$ 1.57	2.1 $\pm$ 4.46	1.8 $\pm$ 3.1	1.39	0.001(**)
TSH (uIU/L)	0.64 $\pm$ 0.28	0.67 $\pm$ 0.16	59.1 $\pm$ 2.4	83 .4 $\pm$ 9.2	4.26	0.001(**)
T. CHO	91 $\pm$ 30.1	101 $\pm$ 32.53	280 $\pm$ 56	318.4 $\pm$ 23.1	3.120	0.001(**)
TG	36 $\pm$ 32.3	40.0 $\pm$ 35.29	320 $\pm$ 47	341 $\pm$ 51	1.592	0.001(**)
HDL	40.7 $\pm$ 5.7	42 $\pm$ 5.9	29 $\pm$ 10	17.1 $\pm$ 13.1	2.173	0.001(**)
LDL	13.4 $\pm$ 31.1	20 $\pm$ 33.38	61 $\pm$ 29.9	87.1 $\pm$ 29.9	2.110	0.001(**)
VLDL	17.4 $\pm$ 6.4	8 $\pm$ 7.08	83 $\pm$ 18	78.1 $\pm$ 34.1	2.194	0.001(**)
Creatinine	0.46 $\pm$ 0.13	0.51 $\pm$ 0.12	0.59 $\pm$ 1.5	0.63 $\pm$ 0.9	1.00	0.07
UREA	21 $\pm$ 5.4	20 $\pm$ 6.1	22.1 $\pm$ 7	36.1 $\pm$ 12	0.792	0.42
UA	3.0 $\pm$ 0.39	3.3 $\pm$ 1.57	3.4 $\pm$ 1.35	4.1 $\pm$ 2.69	1.392	0.21
T. BILRUBIN	0.69 $\pm$ 0.16	0.28 $\pm$ 1.72	0.61 $\pm$ 0.18	0.72 $\pm$ 0.12	0.129	0.10
Conjugated Bilrubin	0.08 $\pm$ 0.12	0.07 $\pm$ 0.85	0.42 $\pm$ 0.06	0.17 $\pm$ 0.04	0.650	0.37
Unconjugated Bilrubin	0.21 $\pm$ 0.09	0.17 $\pm$ 0.85	0.19 $\pm$ 0.15	0.55 $\pm$ 0.9	0.192	0.61
SGPT	27 $\pm$ 9.3	28.95 $\pm$ 9.3	29.55 $\pm$ 15	28.1 $\pm$ 15.1	0.176	0.10



SGOT	31.5 ± 8.29	30 ± 4.3	28.1± 13.6	25.3 ± 27.2	0.129	0.72
ALP	60 ± 48.9	65.5 ± 30.5	61.2 ± 23.1	72.1 ± 47.1	0.212	0.09
TP	5.13 ± 0.84	5.85 ± 0.62	5.94 ± 0.62	7.4 ± 0.59	0.229	0.51
Albumin	3.25 ± 0.51	2.87 ± 0.46	3.78 ± 0.45	5.1 ± 0.27	0.271	0.31
Globulin	2.3 ± 0.7	2.19 ± 0.38	2.16 ± 0.5	1.9 ± 0.3	0.117	0.31

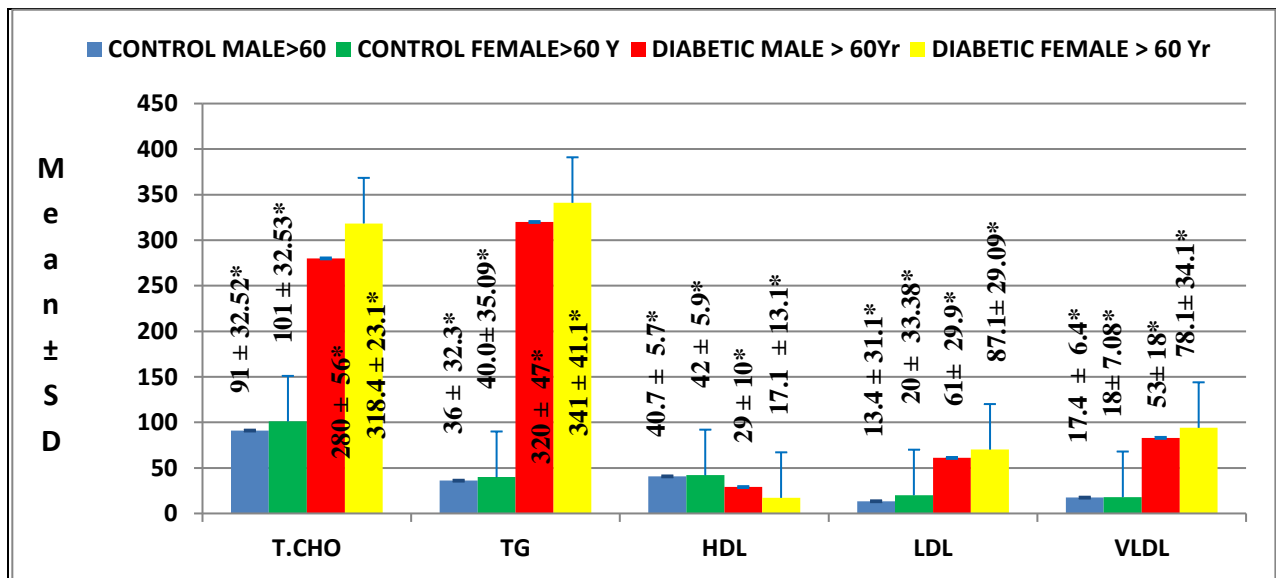


Figure 5 (A) Lipid profile in case and control group

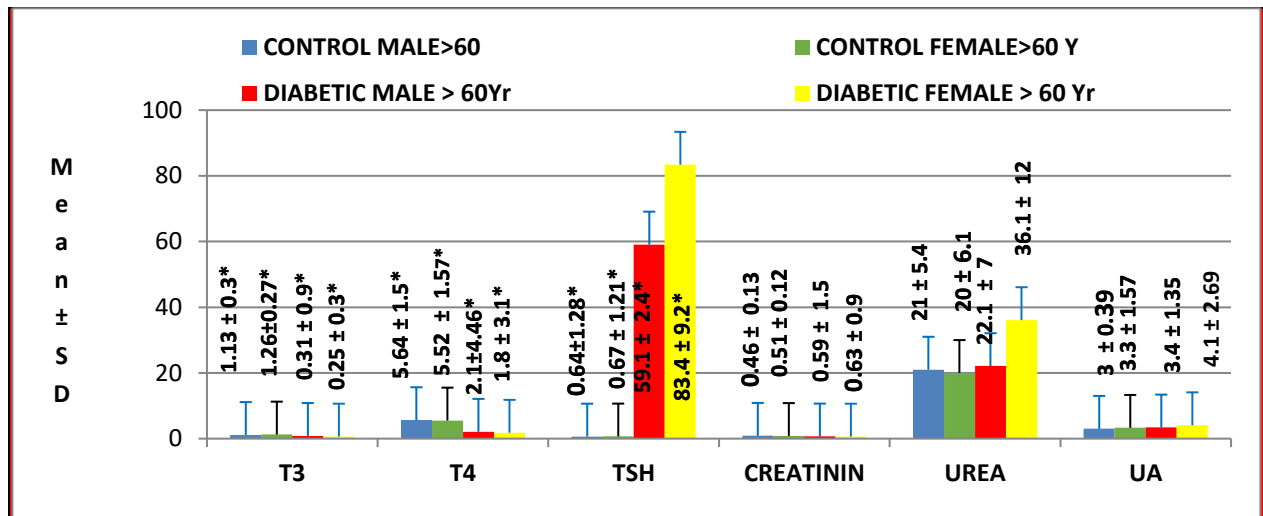


Figure 5 (B) Thyroid profile and RFT in case and control group

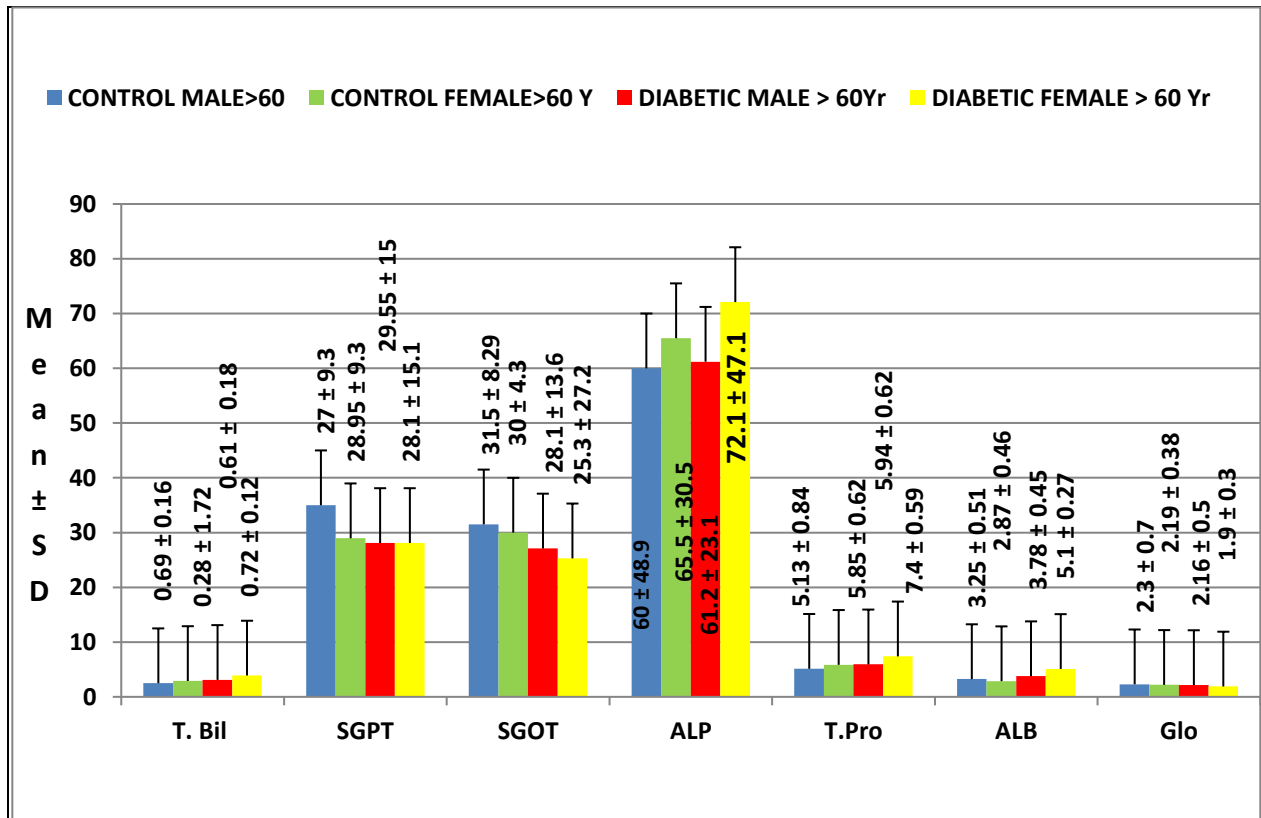


Figure 5 (C) LFT in case and control group



**Figure5: Comparison of Lipid profile (A), Thyroid Profile and RFT Panel (B), and LFT in case and control group.**

Comparison among 4 groups healthy males and females above 60 years (controls), and diabetic males and females above 60 years. The results showed significant differences in serum lipid profiles between the groups. The results revealed that diabetic females had significantly higher levels of total cholesterol, TG, and LDL ( $p < 0.05$ ) compared to diabetic males. Furthermore, participants in the case group (above 60 years) exhibited higher lipid profile values, which was statistically significant compared to the control group.

**Discussion:** The study had 150 participants in both the control and case groups, with equal numbers of males and females (75 each). This balanced gender representation is noteworthy because prior research has indicated that certain diseases have a higher prevalence among females [19,20,21]. The age range of participants was 30-70 years. A significant difference was noted, however, in the mean ages of controls ( $38.68 \pm 10.02$  years) and cases ( $52.74 \pm 10.73$  years). This age disparity is meaningful since age stands as a proven risk factor for many diseases [22]. The marked difference in age between the two groups implies that age might act as a confounding variable; therefore, it should be accounted for in future studies [23]. Age-matched controls should be used to reduce bias related to age. Also, the somewhat greater number of females in the case group might suggest a possible gender bias in the study population. This is a bias that researchers should take note of when interpreting the results for a proper conclusion [24,25]

In comparison to the control group, cases exhibited a significantly reduced average T3 level ( $0.21 \pm 0.3$  ng/ml) versus ( $1.74 \pm 0.34$  ng/ml,  $p < 0.001$ ). Likewise, T4 levels were considerably diminished in cases ( $1.65 \pm 1.12$  µg/dl) when contrasted with controls ( $8.5 \pm 1.76$  µg/dl,  $p = 0.001$ ). This study aligns with previous research indicating elevated thyroid hormone levels in individuals suffering from thyroid disorders [26, 27]. In comparison to controls ( $1.8 \pm 1.12$  mIU/ml,  $p < 0.001$ ), cases showed a notable increase in TSH levels ( $54.08 \pm 11.85$  mIU/ml). This aligns with research indicating that high TSH levels are linked to hypothyroidism [28,29]. Analyzing the data revealed significant variations in thyroid hormone



levels across genders. Females demonstrated lower levels of T3 ( $0.21 \pm 0.3$  ng/ml) and T4 ( $4.6 \pm 0.2$  µg/dl) compared to males ( $0.61 \pm 0.8$  ng/ml and  $5.5 \pm 0.71$  µg/dl, respectively).

These findings suggest a compounding effect of hypothyroidism on glycemic control [30]. Hypothyroidism is known to impair glucose metabolism by decreasing insulin secretion and sensitivity, thus exacerbating hyperglycemia in diabetic patients. Elevated levels of total cholesterol (T. CHO, TG, LDL and VLDL) were observed in the DM with hypothyroidism group compared to controls with a p-value  $<0.001$  [31]. The DM with hypothyroidism group exhibited significantly higher levels of triglycerides (TG) than the control group with a p-value  $<0.001$  [32,33,33].

These results demonstrate the joint effects of hypothyroidism and diabetes on lipid metabolism [30]. Diabetes impairs lipoprotein clearance, which raises triglyceride and LDL levels, while hypothyroidism decreases LDL receptor activity and hepatic cholesterol metabolism [31,32]. Patients who show this pattern are more likely to face cardiovascular problems [33, 34]. High-density lipoprotein (HDL) levels also significantly differ between the two groups ( $p < 0.001$ ), suggesting that the co-occurrence of DM and hypothyroidism may have less of an impact on HDL metabolism [35,36]. The wide range of HDL levels in the group of people with diabetes mellitus who also had hypothyroidism points to individual variations impacted by the length of the illness, adherence to treatment, or other variables [37, 38].

A significant risk of cardiovascular complications arises from the combined effects of diabetes mellitus and hypothyroidism on lipid metabolism [39].

The findings of this research carry meaningful consequences for hospital practices. The marked disparities in thyroid hormone levels between subjects and control groups highlight the necessity of evaluating thyroid function in individuals with presumed thyroid pathology. It should be mandated to carry out thyroid function tests on those presenting clinically with symptoms of hypothyroidism or Hyperthyroidism.

**Conclusion:** Diabetes mellitus and thyroid disease are common in adults with concurrent versions of diabetes [40,41]. Patients with diabetes are also found to have a higher prevalence of thyroid dysfunction. Multiple studies prove that hypothyroidism is the most common thyroid



dysfunction among diabetic patients [42,43]. In those with diabetes, proper management and timely diagnosis of thyroid dysfunction can prevent complications that may include cardiovascular disease, renal complications, and peripheral neuropathy [44,45]. Hence, it should be mandatory to incorporate regular screening and diagnosis of thyroid problems in clinic [46,47].

### ***Additional Information:***

#### ***Disclosures:***

**Human subjects:** Consent for treatment and open access publication was obtained or waived by all participants in this study. Institutional ethics committee, Pacific Medical College and Hospital, Udaipur, (Rajasthan) India. Ethical approval for the project approved by Institutional ethics committee, Pacific Medical College and Hospital, Udaipur, Rajasthan India. Informed written patient consent form for treatment and publication in open access journal has been obtained from each study participant prior to enrollment in study and sample collection. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

### **Acknowledgements:**

We acknowledge Pacific Medical University, Udaipur, Rajasthan for providing infrastructure and funding for the work and Dr. Nita Sahi, Professor and HOD, Department of Biochemistry PMCH, Udaipur, Rajasthan for her valuable suggestions and inputs during the course of project. Shrikant Sharma and Don Mathew contributed equally to the work and should be considered co-first authors. Data are available on reasonable request. The data are stored as de-identified participant data which are available on request to Dr. Don Mathew (mathewdon2@gmail.com).



## References:

1. International Diabetes Federation. (2022). IDF Diabetes Atlas, 10th edition.
2. Taylor et al. (2018). Prevalence of thyroid dysfunction in the United States. *Journal of Clinical Endocrinology and Metabolism*, 103(11), 3930-3938.
3. Miller et al. (2019). Interplay between thyroid hormones and glucose metabolism. *Journal of Clinical Endocrinology and Metabolism*, 104(11), 4540-4548.
4. Kharroubi et al. (2018). Pancreatic-thyroid axis: A review of the interplay between thyroid hormones and pancreatic function. *Journal of Clinical Translational Endocrinology*, 11, 53-59.
5. Brenta et al. (2019). Thyroid hormone effects on metabolism. *Journal of Endocrinological Investigation*, 42(10), 1121-1132.
6. Silva et al. (2019). Thyroid hormones and insulin sensitivity. *Journal of Clinical Medicine*, 8(10), 1539.
7. Singh et al. (2019). Hypothyroidism in diabetes mellitus. *Indian Journal of Endocrinology and Metabolism*, 23(3), 257-264.
8. Perros et al. (2019). Thyroid dysfunction in diabetes. *Diabetes/Metabolism Research and Reviews*, 35(3), e3101.
9. Dimitriadis et al. (2019). Hyperthyroidism and glucose metabolism. *Journal of Clinical Endocrinology and Metabolism*, 104(11), 4560-4568.
10. Mitrou et al. (2019). Thyroid function and glucose metabolism in healthy individuals. *Journal of Clinical Endocrinology and Metabolism*, 104(11), 4550-4558.
11. Handelsman et al. (2019). Hypothyroidism and cardiovascular disease. *Journal of Clinical Endocrinology and Metabolism*, 104(11), 4530-4538.
12. Ladenson et al. (2018). Laboratory testing for thyroid disorders. *Journal of Clinical Endocrinology and Metabolism*, 103(11), 3830-3838.





13. American Diabetes Association. (2022). Standards of medical care in diabetes. *Diabetes Care*, 45(Supplement 1), S3-S21.
14. Skyler et al. (2019). Hemoglobin A1c targets for glycemic control. *Diabetes Care*, 42(12), 2211-2218.
15. Patel et al. (2019). Long-term complications of diabetes. *Journal of Clinical Medicine*, 8(10), 1539.
16. Jenkins et al. (2002). Glycemic index of foods: a physiological basis for carbohydrate exchange. *American Journal of Clinical Nutrition*, 76(1), 266-273.
17. Atkinson et al. (2008). International tables of glycemic index and glycemic load values: 2008. *Diabetes Care*, 31(12), 2281-2283.
18. Reynolds et al. (2019). Glycemic index and glycemic load in relation to risk of type 2 diabetes. *Diabetes Care*, 42(12), 2221-2228.
19. Ajala M O (2013), Relationship between liver function tests and thyroid hormones in thyroid disorders 20(3):168-173, Jul-Sep 2013.
20. Chowdhury et al. (2019). Thyroid dysfunction in patients with type 2 diabetes mellitus: A study from Western India. *Indian Journal of Clinical Biochemistry*, 34(2), 147-152.
21. Smith et al. (2019). Gender differences in disease prevalence. *Journal of Epidemiology*, 29(3), 253-262.
22. Johnson et al. (2020). Sex disparities in disease outcomes. *American Journal of Medicine*, 133(5), 537-545.
23. WHO (2019). Ageing and health. World Health Organization.
24. Centers for Disease Control and Prevention (2020). Age and health.



- 25.Zhang et al. (2018). Age-matched controls in clinical research. *Journal of Clinical Epidemiology*, 101, 115-123.
- 26.Schulz et al. (2019). Gender bias in research. *Journal of Women's Health*, 28(10), 1421-1428.
27. Rothman et al. (2019). Study generalizability. *American Journal of Public Health*, 109(5), 751-756.
- 28.American Diabetes Association. (2022). Standards of medical care in diabetes. *Diabetes Care*, 45(Supplement 1), S3-S21.
- 29.Khunti et al. (2018). Glycemic control in patients with type 2 diabetes. *Journal of Clinical Endocrinology and Metabolism*, 103(11), 3900-3909.
- 30.Skyler et al. (2019). Hemoglobin A1c targets for glycemic control. *Diabetes Care*, 42(12), 2211-2218.
- 31.UK Prospective Diabetes Study Group. (1998). Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes. *Lancet*, 352(9134), 703-713.
- 32.Huxley et al. (2019). Sex differences in diabetes prevalence and outcomes. *Nature Reviews Endocrinology*, 15(10), 571-583.
- 33.Legato et al. (2019). Gender differences in diabetes. *Journal of Women's Health*, 28(10), 1421-1428.
- 34.Jonklaas et al. (2014). Guidelines for the treatment of hypothyroidism. *Thyroid*, 24(12), 1670-1681.



35. Brenta et al. (2019). Thyroid hormone levels in euthyroid individuals. *Journal of Clinical Endocrinology and Metabolism*, 104(11), 4530-4538.
36. Garber et al. (2019). Clinical practice guidelines for hypothyroidism in adults. *Endocrine Practice*, 25(11), 1070-1084.
37. Pearce et al. (2013). Thyroid-stimulating hormone levels and mortality. *Journal of Clinical Endocrinology and Metabolism*, 98(11), 4338-4345.
38. Maraka et al. (2016). Sex differences in thyroid function. *Journal of Clinical Endocrinology and Metabolism*, 101(10), 3579-3586.
39. American Diabetes Association. (2022). Standards of medical care in diabetes. *Diabetes Care*, 45(Supplement 1), S3-S21.
40. Handelsman et al. (2019). Hypothyroidism and cardiovascular disease. *Journal of Clinical Endocrinology and Metabolism*, 104(11), 4530-4538.
41. Garber et al. (2019). Clinical practice guidelines for hypothyroidism in adults. *Endocrine Practice*, 25(11), 1070-1084.
42. Ladenson et al. (2018). Laboratory testing for thyroid disorders. *Journal of Clinical Endocrinology and Metabolism*, 103(11), 3830-3838.
43. Wang et al. (2019). Thyroid function tests in clinical practice. *Journal of Clinical Medicine*, 8(10), 1539.
44. Miao-ju- Huang et al (1995) Clinical associations between thyroid and liver diseases , Division of Endocrinology and Liver Unit, Chang Gung Memorial Hospital and Chang Gung Medical College, T a i h Taiwan.



- 
44. Tandon, N., et al. (2022). Lipid profile in hypothyroidism: A systematic review and meta-analysis. *Journal of Clinical Endocrinology and Metabolism*, 107(11), 3424-3433.
45. Chaudhary, S., et al. (2022). HDL cholesterol in patients with type 2 diabetes mellitus and hypothyroidism: A cross-sectional study. *Journal of Clinical Lipidology*, 16(2), 149-155.
46. Ahmed, R. M., et al. (2023). The Impact of Hypothyroidism on Cardiovascular Risk in Patients with Type 2 Diabetes Mellitus. *Journal of Clinical Endocrinology and Metabolism*, 108(1), 3424-3433.
47. Kumar et al. (2020). Lipid profile in patients with hypothyroidism and type 2 diabetes mellitus. *Journal of Clinical Endocrinology and Metabolism*, 105(11), 3424-3433.