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ASTUDY ON SYNERGISM OF THYROID DISORDERS AND TYPE2 DIABETES MELLITUS.

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ABSTRACT

BACKGROUND & OBJECTIVES:

Thyroid hormones are important regulators of glucose homeostasis. However, the association between thyroid hormones within the reference range and type 2 diabetes mellitus (T2DM) remains unclear. Thyroid dysfunction and diabetes mellitus are closely linked. Several studies have documented the increased prevalence of thyroid disorders in patients with diabetes mellitus and *vice versa*.Thyroid dysfunction (TD) and diabetes mellitus (DM) are two of the most frequent chronic endocrine disorders with variable prevalence among different populations. The aim of this study was to clarify the incidence of T2DM according to the baseline levels and changes of thyrotropin (TSH) and thyroid hormones (free thyroxine and triiodothyronine) in euthyroid subjects.

MATERIALS

METHODS: AcasecontrolstudywasconductedintheDepartmentofBiochemistry,MahatmaGandhiMemorialHospital,WarangalduringDecember2016toMay2018.Atotalof60subjectswereincludedinthestudyanddividedinto2groupswith30healthycontrolsand30diabetics.Fastingplasmaglucose,Fastinglipidprofile,thyroidprofilewereestimatedwithbloodsamplesdrawnunderasepticconditionsandtheirBMIwascalculated.Anindependentt-testwasusedtocomparemeanvaluesofeachparameteramongthegroups.Toobservepossiblerelationshipsbetweenparameters,Pearson'scorrelationcoefficient(r)wasused.

RESULTS:T_3&T_4mean±SDvalues(116.2±20.49;5.60±2.32)werelowindiabeticpatientscomparedtonon-diabeticcounterparts(124.23±29.97;5.60±2.32)whereasTSHlevelswereelevated(5.58±1.52)india

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beticpatientscomparedtonormal(1.87±0.79)controls.ThereweresignificantpositivecorrelationsbetweenFBGandTSHandnegativecorrelationsbetweenFBGandT_3andT_4indiabetics.Thereweresignificantpositivecorrelationsbetween TSHandTC,LDL-CandTG,andnegativecorrelationsbetweenTSHandHDL-Cofdiabeticsandthereweresignificantpositivecorrelationsbetween TSHandBMIandnegativecorrelationsbetweenT_3andT_4withBMIofT2DMstudysubjects.

CONCLUSION: Thepresentstudysuggeststhattheabnormalthyroidhormonelevelsseenintype2diabeticsareduetoalterationinhypothalamo–pituitary–thyroidaxis,whichinturnproducessignificantmetabolicdisturbances.Thyroiddysfunctionwasassociatedwithworseningdyslipidemiaintype-2diabeticindividuals.Hence,routinescreeningforthyroiddysfunctionshouldbecarriedoutindiabetics,whichhelpsinitsearlydiagnosisandtreatmenttherebyimprovestheirqualityoflifeandreducesthemorbidityrate.

Keywords: DiabetesMellitus,Hypothyroidism,DyslipidemiaandBMI.

INTRODUCTION

Diabetes mellitus and thyroid dysfunction are intimately related.The two most prevalent chronic endocrine illnesses are thyroid dysfunction (TD) and type 2 diabetes mellitus, with multiple frequencies within various populations.[1]Numerous studies have shown that thyroid issues are more common in those with diabetes mellitus and vice versa. The present level of knowledge on the central and peripheral influence of thyroid hormone on food intake and glucose and lipid metabolism in target tissues (such as liver, white and brown adipose tissue, pancreatic cells, and skeletal muscle) to explain the mechanism connecting overt and subclinical hypothyroidism to type 2 diabetes and metabolic syndrome.

Definition of metabolic syndrome:For the purposes of this investigation, the diagnosis of metabolic syndrome was done based on the modified Asian NCEP-ATP III panel criteria. Modified Asian ATP III standards are identical to the original ATP III criteria, with the exception of a waist circumference (WC) more than 90 cm for men and 80 cm for women. A diagnosis can only be made if three out of the following five risk factors are present: abnormal WC, TG levels over 150.0 mg/dL or pharmaceutical therapy (Rx), male and female HDL-C levels below 40.0 mg/dL or Pharmaceutical Treatment, blood pressure above 130 mm Hg systolic and above 85 mm Hg diastolic or Pharmaceutical Treatment, and FBG concentration above 100.0 mg/dL. [2] Definition of thyroid dysfunction and euthyroid:Subjects were categorised into one of the five groups described below based on guidelines for the use of thyroid function testing.

(1) A normal thyroid function test was used to define euthyroid.

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(2) A TSH level of less than 0.40 IU/mL combined with an increased fT4 and fT3 level was considered hyperthyroid.

(3) TSH less than 0.40 IU/mL with normal fT4 and fT3 concentrations was deemed to be subclinical hyperthyroidism.

(4) A TSH level more than 4.20 IU/mL and a fT4 and fT3 concentration below normal were considered hypothyroidism.

(5) SCH was classified as having a TSH level more than 4.20 IU/mL and normal fT4 and fT3 levels.[3]

The most effective blood test combination for diagnosis and follow-up of both ambulatory and hospitalised patients, according to the American Thyroid Association, is TSH and fT4.The first studies establishing the link between thyroid malfunction and diabetes were published in 1979. Since then, several studies have been done in numerous nations in an effort to determine the incidence of thyroid dysfunction among diabetes patients. Between 2.2 and 17 percent of diabetics are said to have thyroid problems. Another study found that individuals with Type 2 Diabetes mellitus (T2D) had a significant prevalence of abnormal TSH levels (31 percent).

Additionally, women with diabetes are afflicted more often than males, and hypothyroidism is more prevalent than thyrotoxicosis. It has been demonstrated that almost one in twenty women with Type 2 Diabetes mellitus experience subclinical hypothyroidism. Adults in Europe and the United States have a prevalence of thyroid disease of 6.6%; it rises with ageing and affects more women than men.[4,5] In response to appropriate tissue levels of TH, T3, the active thyroid hormone (TH), produces a drop in TRH and TSH production at the level of both thyrotrophs in the pituitary and tanycytes in the hypothalamus.Tanycytes are located in the ventral walls of the 3rd ventricle in the mediobasal hypothalamus (MBH), function as gatekeepers. Tanycytes are able to transport, sense, and modify the release of hormones of the hypothalamus pitiuitary thyroid axis and are involved in feedback regulation. Therefore, subclinical hyperthyroidism (SHyper) and subclinical hypothyroidism (SHypo) are both characterised by low or elevated serum TSH, with TH levels at the upper and lower ranges of their reference range, respectively.Since 1980, the prevalence of this illness in the adult population throughout the world has increased from 4.7 percent to 8.5 percent. According to the National Health and Nutrition Examination Survey (NHANES) III, 14% of adult US citizens have either diabetes mellitus (DM) or impaired fasting blood sugar levels. According to data from the Centers for Disease Control and Prevention's National Diabetes Fact Sheet, Type 2 Diabetes Mellitus may go undetected often; in the United States, prediabetes may affect up to 35% of persons over 20 and 50% of those over 65.Type 2 Diabetes mellitus and thyroid disease are two closely

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associated disorders. The NHANES III study reported a higher prevalence of TD in subjects in the United States with diabetes compared with those without diabetes, especially in patients with positive anti-thyroperoxidase (TPO) antibodies . [6,7,8]

According to estimates, 382 million people worldwide had diabetes in 2013, with 90 to 95 percent of those having Type 2 Diabetes mellitus. In nations like China, Oceania, South and Central Asia, Latin America, and the Middle East, there is an epidemic risk of Type 2 Diabetes mellitus, and the prevalence of DM is predicted to rise to 592 million by 2035, developing in 7.8 percent to 8.8 percent of people.[6,7]In the early stages of the condition, cells increase insulin production to counteract insulin resistance and guarantee proper glucose absorption and metabolism in peripheral organs. The advent of overt Type 2 Diabetes mellitus in adults, however, might result in postprandial hyperglycemia because cells cannot maintain prolonged hyperinsulinemia. Insulin resistance can be a component of the metabolic syndrome (MetS), a collection of cardiovascular and metabolic disorders.[9]

Hyperthyroidism and Type 2 Diabetes mellitus:4.4 percent of adult patients with Type 2 Diabetes mellitus had hyperthyroidism, compared to 2 to 4 percent of T2 patients with diabetes who had the condition. This is greater than the prevalence of the condition in the general population. Females were more likely than males to receive a new diagnosis of subclinical hyperthyroidism in Type 2 Diabetes mellitus patients (4.3 percent vs. 3.5 percent), and the relative risk was substantially greater in women exclusively. It appears that toxic multinodular goitre is a more prevalent cause of hyperthyroidism than gestational diabetes since advanced age and the presence of goitre are strongly and independently connected with the prevalence of subclinical hyperthyroidism in the population with diabetes. Type 2 Diabetes does not predict the likelihood of becominghyperthyroidism in the elderly population with diabetes.[10,11]

Hypothyroidism and Type 2 Diabetes mellitus : Because hypothyroidism is more common in people with diabetes than in the general population, TH deficit in Type 2 Diabetes mellitus patients is unlikely to be a coincidence. The most prevalent types of thyroid disease in Type 2 Diabetes mellitus and MetS are overt and subclinical hypothyroidism. According to epidemiological research conducted on people from various racial and cultural backgrounds, the incidence of hypothyroidism in Type 2 Diabetes mellitus ranges from 6 to 20 percent. This vast range can be due to variations in the iodine consumption, sex, and age of the people examined. An increased incidence of hypothyroidism in Type 2 Diabetes mellitus T2D is connected with female sex, older age, obesity, TPO Ab positive, and hospitalisation. In individuals with Type 2 diabetes, the risk of hypothyroidism was significantly raised.[10,11]

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Table 1 :Prevalence of Thyroid Diseases in Type 2Diabetes mellitus.[10,11]

Prevalence	Associated Risk Factors
Adults with T2D are at risk for hypothyroidism.	6%–20%
early signs of hypothyroidism	Female sex, TPO Ab^{+}, advanced age, hospitalization
Hypothyroidism risk in T2D older than 65 years old	OR, 4.82 males vs 2.60 females
	OR, 2.56 obese vs 3.11 nonobese
	OR, 4.26 TPO^{+} vs 2.93 TPO^{-}
Subclinical hypothyroidism Risk in T2D	10.2%
Adults with T2D and subclinical hypothyroidism prevalence compared to healthy controls*	1.93-Fold increased risk (95% CI, 1.66–2.24)

Subclinical hypothyroidism is a frequent finding in Type 2 Diabetes mellitus, according to a significant longitudinal research conducted in women with T2D in Australia. It was the most common kind of thyroid hormone deficit among diabetic female patients and those with positive TPO Abs. According to these findings, a meta-analysis of 36 articles found that individuals with Type 2 Diabetes Mellitus had a higher pooled prevalence of Subclinical Hypothyroidism than healthy controls (1.93-fold increased risk; 95 percent confidence interval, 1.66 to 2.24) It was linked to a higher risk of microvascular problems in those with diabetes.[10,11]

Changes in TSH and/or TH in longitudinal studies and incidence of diabetes: Thyroid hormone has a vital role in controlling the hepatic metabolism of hepatic fat, cholesterol, and glucose (TH). Thyroid hormone causes lipogenesis and hepatic lipogenesis. Thanks to advancements in disciplines like cell imaging, autophagy, and metabolomics, the molecular regulation of hepatic lipid metabolism by thyroid hormones is now well understood. Thyroid hormone speeds up the transfer of reverse cholesterol. Thyroid hormone regulates hepatic gluconeogenesis via SirT1 and FoxO1. Recent studies imply that clinical illnesses connected to dysregulation include type 2 diabetes mellitus and non-alcoholic fatty liver disease. Hepatic metabolism may change if TH intracellular activity changes. Additionally, TH is necessary for lipophagy in lipid metabolism, mitochondrial quality control, and the control of the metabolic genes FoxO1 and SirT1.The activities of thyroid hormone in hepatic metabolism, the connection between TH and metabolic diseases, and the possible therapeutic use of thyromimetics to treat metabolic dysfunction in the liver are all topics covered in this study.[12,13]

TSH may have an immediate impact on metabolic parameters and encourage the release of leptin from human adipose tissue. It has stimulatory effects on hepatic glucose production both in vivo and in vitro and plays a significant role in hepatic glucose metabolism. In a mouse liver, TSH stimulates the mRNA expression of glucose 6-phosphate and phosphoenolpyruvate

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carboxykinase (PEPCK). Additionally, TSH raises serum blood glucose levels by decreasing insulin production and its synthesis from pancreatic cells. Leptin regulates the expression of the TRH gene in the paraventricular nucleus (PVN), acting directly on the hypothalamic-pituitary-thyroid (HPT) axis, and indirectly on TRH via actions in the arcuate nucleus (ARC).Patients with hypothyroidism have high leptin levels, which correspond with TSH levels. Additionally, leptin levels are increased in many diabetic individuals, and this may be because leptin affects the HPT axis via the Janus Activating Kinase (JAK)-2/Signal Transducer and Activator of Transcription (STAT)3 factor, which in turn stimulates the synthesis of TSH.[14,15]

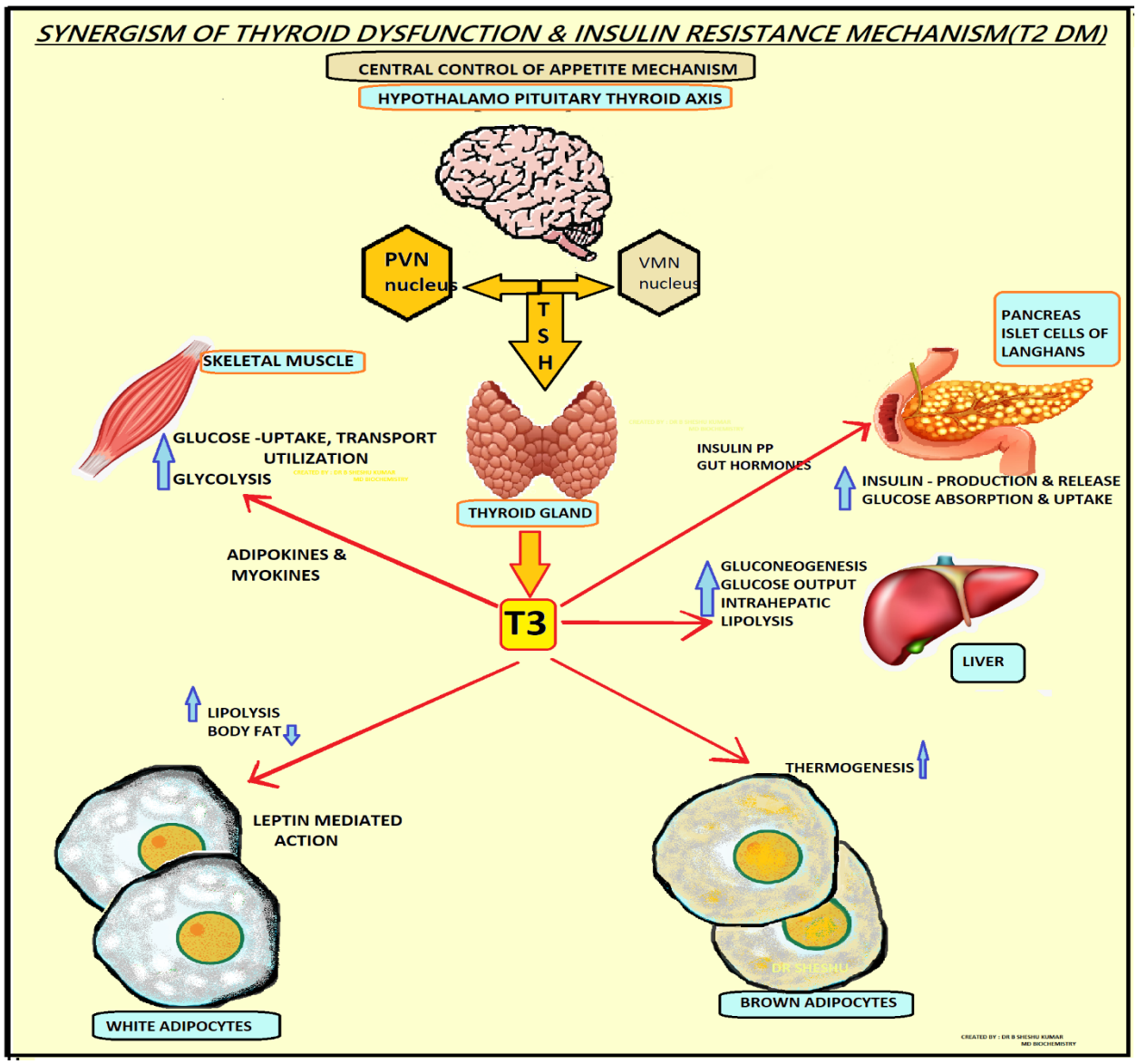

FIGURE 1 : The above figure describes the synergistic mechanism of association of Thyroid disorders and Insulin Resistance mechanism (Type 2 Diabetes Mellitus).

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Regulation of hepatic glucose and lipid metabolism: The formation of healthy pancreatic islets depends on thyroid hormone receptors (TRs) 1 and 1. Neonatal cells have TH receptors, and exposure to T3 determines the transcription factor MAFA's activation, which promotes insulin production and cell maturation. T3 also encourages the growth of pancreatic islet cells. It appears to work as a mitogenic prosurvival factor for pancreatic cells and enhances the production of proinsulin mRNA through a process that appears to entail MAPK/ERK activation.[17]T3 controls how cells behave physiologically. It affects the liver, skeletal muscles, and adipose tissue differentially, which are the primary sites of insulin action, controlling insulin secretion and glucose absorption. Thyroid hormone interacts with insulin synergistically in the peripheral tissues, but insulin-antagonistically in the liver. Thyroid hormone decreases liver sensitivity to insulin by increasing hepatic glucose output through increased hepatic expression of glucose transporter (GLUT)2 and stimulating endogenous glucose synthesis through enhanced gluconeogenesis and glycogenolysis. The transport of alanine into hepatocytes and the conversion of alanine to glucose are both accelerated by thyroid hormone treatment. The increased expression of glucose 6-phosphate mRNA and the production of PEPCK are two significant effects of T3.[18]T3 can also function on the sympathetic route that links the paraventricular hypothalamus to the liver, regulating hepatic glucose production and insulin sensitivity. Independent of plasma T3, insulin, glucagon, and corticosterone, T3 injection in the hypothalamic PVN stimulates hepatic glucose synthesis. The fact that selective hepatic sympathectomy eliminates this effect supports the theory that T3-sensitive neurons in the PVN regulate the generation of liver glucose through sympathetic liver projections. Thyroid hormone induces the mRNA for the 2-adrenergic receptor and suppresses the inhibitory G protein RNA of the adenylate cyclase cascade, which helps epinephrine and glucagon produce the effects of gluconeogenesis and glycogenolysis.

By inducing lipogenic enzymes, T3 worsens the dysregulation of hepatic glucose and lipid metabolism that is indicative of insulin resistance. T3 stimulates both lipogenesis and lipolysis.Through the control of fatty acid transporter proteins and an increase in hepatic lipogenesis, thyroid hormone may boost fatty acid absorption in the liver. The intrahepatic lipolysis brought on by T3 has been linked to the activation of hepatic lipases and lipophagy.

The hyperinsulinemic state is maintained through nonsuppressed gluconeogenesis and the conversion of glucose to fatty acids. Significant islet function impairment is brought on by hyperthyroidism and high-fat diets. Contrarily, physiological T3 administration keeps islet structure, size, and consistency stable and halts streptozocin-induced islet degeneration.[18,19]

AIMS & OBJECTIVES

MATERIALS & METHODS: AcasecontrolstudywasconductedintheDepartmentofBiochemistry,MahatmaGandhiMemorialHospital,WarangalduringDecember2016toMay2018.60subjectswereincludedinthestudyfromDepartmen

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tofEndocrinologyandDepartmentofInternalmedicine,MahatmaGandhiMemorialHospital,Warangal.Inthepresentstudytheindividualsincludedwerecategorizedinto2groups , with 30 in each group.Allthesubjectswereinthe25-75yearsofagegroupandofeithersex.

Inclusioncriteria: Bothoutpatientsandinpatientswithdiagnosisoftype2diabetesmellituswithnohistoryofthyroiddysfunctionwereselectedbysimplerandomsamplingmethod.Controls:Healthycontrolsintheagegroup25-75years.Cases:Diagnosedtype2diabetesmellituspatientsintheagegroup25-75yearswithnopreviousthyroiddysfunction.

Exclusioncriteria: Patientsoftype1diabetesmellitus,knownhistoryofthyroiddysfunction,ondrugsaffectingthyroidfunction,acutelyillcriticalpatientsandthosewithpregnancywereexcludedfromthisstudy.Thestudyalsoexcludedsubjectswhohadundergonethyroidectomy,amputationandthosewhohadagoiter.Diabeticsandcontrolsubjectswithrenalorliverdiseasesoranyotherseriousillnesseswereexcludedfromthestudy.

Specimencollection:Fastingvenousbloodsampleswerecollectedfromallgroups.3mlofbloodwascollectedintoserumvacutainer(redcap)[forlipidprofile],2mlintosodiumfluoridevacutainer(greycap)&another4mlofbloodwascollectedintoserumvacutainer(redcap)[forthyroidprofile].Fastingplasmaglucosewasestimatedinplasma,dailyfromthegreyvacutainerwhileallotherparameterswereestimatedinserum.Lipid&thyroidprofilewasestimatedinfreshseraonadailybasis.

RESULTS

The present study was undertaken in the Department of Biochemistry, Kakatiya Medical College MGM hospital, Warangal. A total of 60 patients were recruited for the study which included 30 T2DM patients without Thyroid dysfunction and 30 healthy non diabetic individuals as controls.Thecaseandthecontrolgroupswereagematchedandsex-matched.

Table2: Demographicdistributionofpatients(ageandsex)incontrol

Sex	**Number**	**AgeMean**	**SD**	**Minimum**	**Maximum**
Male	19	44.83	16.59	27	73
Female	11	38.5	8.77	25	50

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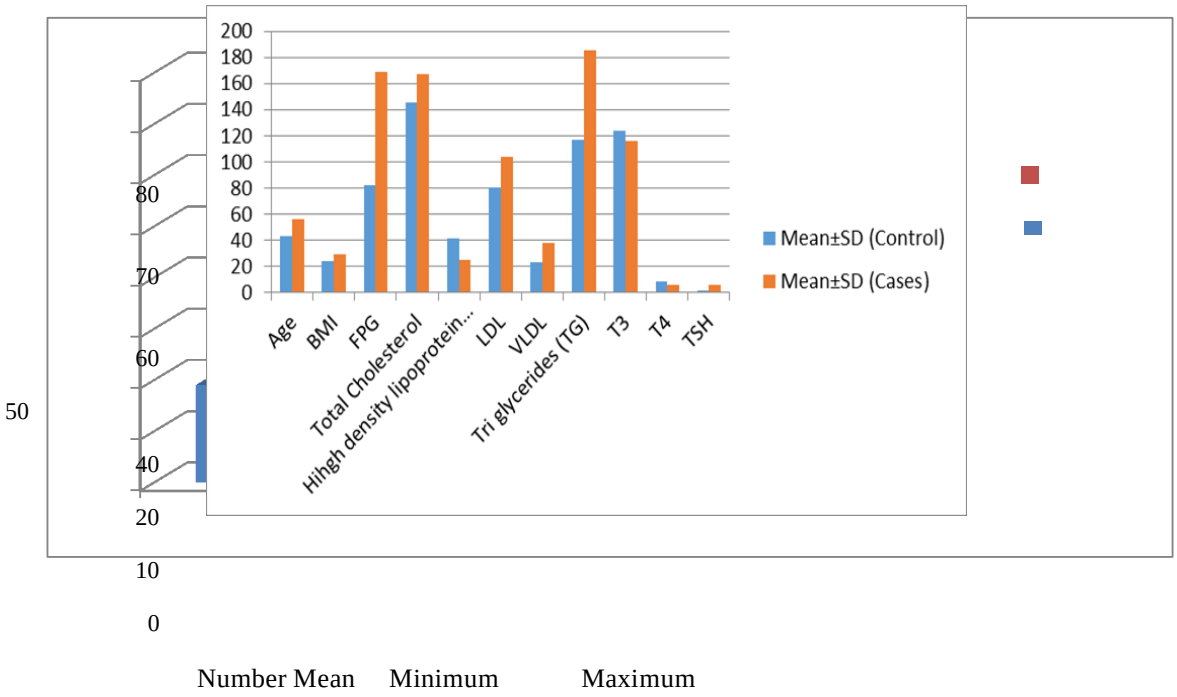

Figure2: Demographicdistributionofpatients(Sexandage)incontrol

Figure3: Distribution of the various variables in the study.

Table3: Demographicdistributionpatients(Sexandage)incases

Sex	**Number**	**AgeMean**	**SD**	**Minimum**	**Maximum**
Male	17	57.06	8.07	44	74
Female	13	53.61	6.64	42	65

Table 4 : Mean and SD distribution of variables in cases and controls.

Parameter	**Mean±SD(Control)**	**Mean±SD(Cases)**
Age	43.23±14.81	56.00±7.86
BMI	24.44±2.61	27.33±3.57
FPG	82.46±11.01	168.5±61.84
TotalCholesterol	145.23±23.15	167±35.55

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Hihghdensitylipoprotein(HDL-C)	41.43±6.89	25.13±5.31
LDL-C	80.46±22.13	104.16±31.03
VLDL-C	23.33±6.21	37.7±7.48
Triglycerides(TG)	116.86±30.94	185.26±33.71
T_3	124.23±29.97	116.2±20.49
T_4	8.23±1.86	5.60±2.32
TSH	1.87±0.79	5.58±1.52

Table 5 : CorrelationbetweenFastingbloodglucoseVsThyroidhormonelevel(Cases)

Thyroidhormone	rvalue
T_3	-0.639
T_4	-0.426
TSH	0.653

**Alltheparametersconsideredtablevalueforcorrelationcoefficient.

Table 6: CorrelationbetweenBMIVsThyroidhormonelevels(Cases)

Thyroidhormone	rvalue
T_3	-0.451
T_4	-0.429
TSH	0.059

**Alltheparametersconsideredtablevalueforcorrelationcoefficient.

Table 7: Correlationbetweenlipidparameterswiththyroidhormonelevels(Cases)

Lipid profile parameter	**T_3(rvalue)**	**T_4(rvalue)**	**TSH(rvalue)**
Totalcholesterol	0.304	0.270	0.356
HDL	0.018	0.000	0.078
LDL	0.296	0.291	0.332
VLDL	0.818	0.767	0.261
Triglycerides	0.818	0.767	0.176

**Alltheparametersconsideredtablevalueforcorrelationcoefficient.

TheMean±SDofalltheparametersstudiedinthetotalcasesweresignificantlydifferentfromthoseofcontrols.Thediabetesgrouppresentedwithsignificantlyhigherlevelsoffastingbloodglucose(168.5±61.84)comparedtotheirnon-diabeticcounterparts(82.46±11.01)whichwasstatisticallysignificant=pvalue<0.001**Thediabetes

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grouppresentedwithsignificantlyhigherlevelsofBMI(27.33±3.57)comparedtotheirnon-diabeticcounterparts(24.44±2.61)whichwasstatisticallysignificantpvalue<0.001** Thediabetesgrouppresentedwithhighermeanvaluesofdyslipidemiaparameters(Totalcholesterol167.00±35.55;LDL104.16±31.03;VLDL37.7±7.48;Triglycerides185.26±33.71)comparedtotheirnon-diabeticpatients(Totalcholesterol145.23±23.15;VLDL23.33±6.21;LDL80.46±22.13;Triglycerides116.86±03.94) whichwasstatisticallysignificant).

Inthepresentstudyallthedyslipidemiaparameterswereelevatedindiabetespatientsexcept HDL.HDLshowedhighervaluesinnormalcontrolpatientsthanthediabeticcases.Inthepresentstudyboth T_3 mean±SDvalues(116.2±20.49)werelowindiabeticpatientscomparedtonon-diabeticcounterparts(124.23±29.97)whichwasstatisticallysignificantpvalue<0.0001*** InthepresentstudyT4mean±SDvalues(5.60±2.32)werelowindiabeticpatientscomparedtonon-diabeticcounterparts(8.23±1.86)whichwasstatisticallysignificantpvalue<0.05.* TSHlevelswere elevated(5.58±1.52)indiabeticpatientscomparedtonormal(1.87±0.79)controlwhichwasstatistically significantpvalue<0.001** Inpresentstudy,Pearsoncorrelationtest,showedthattherewere significantpositivecorrelationsbetweenFBGandTSHandnegativecorrelationsbetweenFBGand T_3 and T_4 ofT2DMstudysubjects

.Inpresentstudy,Pearsoncorrelationtest,showedthattherewere significantpositivecorrelationsbetweenTSHandTC,LDL-CandTG,andnegativecorrelationsbetweenTSHandHDL-CofT2DMstudysubjects.Inpresentstudy,Pearsoncorrelationtest,showsthattherewere significantpositivecorrelationsbetweenTSHandBMIandnegativecorrelationsbetween T_3 and T_4 withBMIofT2DMstudysubjects.

DISCUSSION

Although the greater frequency of thyroid dysfunction in T2DM is noteworthy for the thyroid condition itself, there may also be important implications for the management of diabetes.Patients with T2DM should only be examined for thyroid illness at the time of diagnosis, according to the British Thyroid Association.Whether or whether they have diabetes, everyone over the age of 35 should get a thyroid problem screening every five years, according to the American Thyroid Association.This research may not be generalizable because it is based on a cost-utility study utilising a computer-based decision model for the US healthcare system.[20,21]

In an older population-based sample with type 2 diabetes, thyroid dysfunction was evaluated. According to a research by Gopinath et al., 7.1 percent of people with type 2 diabetes incidentally had thyroid dysfunction, compared to 3.8 percent of people without diabetes (odds ratio 1.97, 95 percent confidence range 0.88-4.38). [22]There was no difference in the frequency of subclinical hypothyroidism between patients with T2DM and controls, according to Ishay et al.[23]

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Adjusted pooled prevalence of SCH was 10.2% in T2DM patients, and T2DM was linked to a 1.93-fold increased risk of SCH (95 percent CI: 1.66, 2.24). Furthermore, Han c et almeta-analysis .Theirstudy found that SCH may have an impact on the development of diabetic complications, with overall ORs for diabetic nephropathy, diabetic retinopathy, peripheral arterial disease, and diabetic peripheral neuropathy of 1.74 (95% CI: 1.34, 2.28), 1.42 (95% CI: 1.21, 1.67), 1.85 (95% CI: 1.35, 2.54), 1.87 (95% CI: 1.06). The authors also came to the conclusion that those with T2DM and subclinical hypothyroidism were more likely to experience diabetic complications and advised that people with T2DM be screened for thyroid problems.[24]

In individuals with TSH >5 mIU/L, the risk of prediabetes rises by 15% (hazard ratio, 1.15; 95 percent CI, 1.04 to 1.26) and the incidence of T2DM increases 1.09-fold with each doubling of TSH mIU/L (95 percent CI, 1.06 to 1.12). According to a research by Brenta et al in a latin American study, MetS is more common in ScH compared to euthyroid persons (OR, 1.31; 95 percent CI, 1.08 to 1.60).[25]According to a research by Meher et al.,[26] the MetS group

had a high frequency of SCH (22%) and overt hypothyroidism (4%). According to a research by Shantha et al.in India, patients with MetS have a significant prevalence of SCH (21.90 percent) and overt hypothyroidism (7.30%).

According to a recent research in Taiwan by Wang et al.[12], 7.21% of Taiwan MetS patients had TD. According to this study, 2.64 percent of participants had subclinical hyperthyroidism and 4.55 percent had SCH. The prevalence of TD was found to be 7.60 percent overall, with 2.10 percent of patients having subclinical hypothyroidism and 5.50 percent having subclinical hyperthyroidism, according to another study conducted in Taiwan by Lai et al.[28] Another research conducted in Turkey by Uzunlulu et al.[29] revealed that 16.40 percent of people there had SCH.However this study did not address patients with overt hypothyroidism and all observations were with SCH patients only.Similar findings were made by Jayakumar et al [30], who discovered that of 120 individuals diagnosed with MetS, 48 had thyroid functions that were normal, 18 had hypothyroidism, 52 had SCH, and two had subclinical hyperthyroidism. SCH and hypothyroidism were found in 60% of individuals with MetS. Another research by Ogbera et al. [31]in Nigeria found that 40.0 percent, 42.0 percent, and 24.0 percent, respectively, of people with hypothyroidism, euthyroidism, and hyperthyroidism also had MetS.

Only fT3 was not substantially affected, indicating that TD was associated with all of the components of MetS. There were significant differences in the mean values for each anthropometric and biochemical parameter between patients with MetS and healthy control participants. These results were consistent with those of Kota et al. [32]who noted that HDL-C was significantly lower in the study group while total cholesterol, low density lipoprotein cholesterol (LDL-C), TG, and TSH were significantly higher in the MetS group when compared to the control group. They also noted that fasting blood glucose (FBG), mean systolic blood pressure (SBP), mean diastolic blood pressure (DBP), mean systolic blood pressure. Another study

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conducted by Meher et al.[26] revealed that the mean SBP, DBP, FBG, total cholesterol, LDL-C, TG, WC, and BMI were considerably higher in the MetS group than in the control group, whereas HDL-C levels were significantly lower. Similar results were found in studies on the Hispanic population conducted by Garduno-Garcia Jde et al. [33]and on the urban population of Chennai conducted by Shantha et al.[27]

Oh et al. [34]discovered a substantial correlation between higher TSH levels within the normal range and the MetS in conjunction with those investigations. TSH levels were substantially correlated with WC, systolic and diastolic blood pressure, and TG, but not with fasting hyperglycemia or low HDL-C levels.Similar to this, Lai et al[28]recent .'s study in Taiwan examined the connection between serum TSH levels and aspects of MetS and came to the conclusion that even small increases in TSH, like those seen in SCH, may be a risk factor for MetS. In that study, TSH levels were significantly higher in the MetS group than in the non-MetS group.To evaluate the odds ratio (OR) of MetS and its components between subclinically hypothyroid and euthyroid groups, Eftekharzadeh A et al. [35]conducted a meta-analysis. The meta-analysis only included trials that used the Adult Treatment Panel III (ATP III) criteria for MetS. Female gender was more abundant in the SCH group [OR = 1.65, 95 percent confidence interval (CI) 1.29-2.13]. Meta-analysis revealed no discernible difference between SCH and euthyroid people in terms of MetS prevalence (OR = 1.13, 95 percent CI 0.95-1.34).According to Giandalia et al. [36] and Triolo's et al[37]. , TSH was strongly correlated withan increased chance of developing type 2 diabetes and visceral obesity due to elevated triglycerides T2DM's sensitivity to atherosclerosis.

Inthepresentstudy30T2DMsubjectsand30healthynondiabeticsubjectswereinvestigatedfortotalT3, totalT4,TSH,FPG,serumcholesterol,serumtriglycerides,serumHDL-C,serumLDL-C,SerumVLDL-CandBMI.Inthepresentstudy,themean±SDofFPGingroup2was168.5±61.84,andinthegroup1was82.46±11.01,thereforefastingbloodglucoselevelwassignificantlyhigher(pvalue<0.001**)indiabetic subjectsascomparedtohealthycontrols,establishingaclearhyperglycemiacondition.

Hyperglycemiaindiabeticpatientsisassociatedwithvasculardamage,impairmentinfunctions ofvariousorganslike;eyes,kidneys,nerves,heartandalsowithendocrineorgans.Thepresentstudyisina ccordancewiththestudiesofSamathaPetal,[38]andReetaTetal.[39]Inthepresentstudy,theMean±SDBMIi nGroup2was27.33±3.57andGroup1was24.44±2.61,whichwassignificantlyhigherindiabeticsubjec ts.pvalue<0.001**Thepresentstudyisinaccordancewith HuFBand MansonJEetal[40]whoshowedthatindividualswithhigherBMIfacedincreasedrisksofdevelopingtype 2DM.Thenonesterifiedfattyacids(NEFAs)secretedfromadiposetissueinobesepeopleleadtothehyp othesisthatinsulinresistanceandβ-

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celldysfunctionaremostlikelylinked.[41]Inthepresentstudy,themean±SDofTotalCholesterolingroup 2(167±35.55)wassignificantlyhigherthangroup1(145.23±23.15)pvalue<0.01.*

ItisinaccordancewithSSRoyandShahPetal[42]whointheirstudyconcludedthatdiabetesisamet abolicderangementaffectingnotonlysugarbutalsolipidmetabolisminvolvingvarioussystemsofbody .MurwanKhalidSabahelkhieretal,[43]observedthattherewasasignificantincreasedlevelsoftotalcholes terol(p=0.001)indiabeticpatientscomparedtonon-diabeticsubjects,thisincreasemaybeduetoanincreaseintheplasmaconcentrationofVLDLandLDL, whichmaybecausedbyincreasinghepaticproductionofVLDLordecreasedremovalofVLDLandLDL fromthecirculation.Kumarnarendraetal[44],reportedthattherewasstatisticallysignificantriseinserumt otalcholesterol(218.11±9.556)indiabeticsascomparedtocontrolsubjects(194.74±8.105).Inthepres entstudy,themean±SDofHDLCholesterolingroup1wassignificantlyhigher(41.43±6.89)thaningrou p2(25.13±5.31)pvalue<0.0001*** Theantiatherogenicpropertiesassociatedwith HDLaredue,atleas tinpart,totheactivityofHDL-associatedenzymes,whichinteractwithLDLandprevent,and/orreverseitsoxidation.[45]

AnumberoffunctionsofHDLparticlesmaycontributetodirectcardioprotectiveeffects,includingpro motionofcellularcholesterolefluxanddirectantioxidativeandanti-inflammatoryproperties.Moreover,lowHDLcholesterollevelsareoftenaccompaniedbyelevatedtrig lyceridelevelsandthecombinationhasbeenstronglyassociatedwithanincreasedriskofCHD.Inconcor dancewiththisstudyRachaiahNM,MalleshappaVR et al [46]intheirstudyobservedthatthemeanvaluesofHDL-Camongmaleandfemalediabetichypertensivesweresignificantlylowerthanthatofcontrolsandconcl udedthatthelowHDLlevelindiabeticsincreasestheriskofcoronaryarterydisease.Recentevidencesug geststhatlowHDLcholesterolisanindependentfactornotonlyforcardiovasculardiseasebutalsoforthe developmentofdiabetesitself.Inthepresentstudy,themean±SDofLDLingroup2(104.16±31.03)was significantlyhigherthaningroup1(80.46±22.13)pvalue<0.0001*** MKSabahelkhier[47]intheirstudy reportedsignificantlyincreasedlevelofLDL(p=0.001)indiabeticpatients.

IncreaseinthenumberofLDLreceptorscausesanincreaseinLDL-cholesterolvalueindiabetesmellitus.Choudhuryetal,intheirstudyobservedahigherLDLcholesteroli nT2DMpatientsincomparisontonon-diabeticcontrolsubjects.Inthepresentstudy,themean±SDofVLDLingroup2(37.7±7.48)wassignific antlyhigherthaningroup1(23.33±6.21)pvalue<0.0001***.AnincreaseinVLDLoccurredindiabetes mellitusduetoincreaseavailabilityofglucoseforVLDLsynthesisanddecreaseinlipoproteinlipaseacti vityleadingtodecreaseofVLDLfromperipheralcirculation.Thenormalinhibitoryeffectofinsulinonh epaticapoBproductionandtriglyceridesecretioninVLDLislost,andtheVLDLsecretedislargerandm oretriglyceride-

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rich.Inthepresentstudy,themean±SDofTAGingroup2(185.26±33.71)wassignificantlyhigherthaningroup1(116.9±30.94)pvalue<0.001**.ThemostcommonalterationoflipoproteinsinT2DMishypertriglyceridemiacausedbyanelevationinVLDLconcentration.InT2DMwithseverehyperglycemia,theclearancerateforLDLapoBisreduced.SarangiRetal[48]reportedthatTC,TG,andLDLweresignificantlyhigher(P<0.001)amongdiabeticsubjectsthancontrols,whereasHDL-Cwasloweramongdiabeticsthanthecontrols(P=0.06).

Inthepresentstudy,thereisahighlysignificantdecreaseinthelevelsofserumT3inT2DMincomparisontothecontrolgroup(pvalue<0.0001***)wherethemean±SDofT3levelingroup2T2DMwas116.2±20.49andingroup1controlwas124.23±29.97.Inthepresentstudy,thereisahighlysignificantdecreaseinthelevelsofserumT4inT2DMincomparisontothecontrolgroup(pvalue<0.05*)wherethemean±SDofT4levelingroup2T2DMwas5.60±2.32andingroup1controlwas8.23±1.86.Inthepresentstudy,thereisahighlysignificantincreaseinthelevelsofserumTSHinT2DMincomparisontothecontrolgroup(pvalue<0.001**)wherethemean±SDofTSHingroup2T2DMwas5.58±1.52andingroup1controlwas1.87±0.79.Regardingthyroidhormones,thepresentstudyrevealedthattheserumlevelofT3,T4wassignificantlylowerinT2DMpatientswhileserumlevelofTSHwassignificantlyhigherinT2DMpatientswhencomparedtothatofnon-diabeticsubjects.Thisisinaccordancewiththestudiesof VikramBVetal [49],GurjeetSetal [50]andShekharCYetal. [51]

Inconcordancetothepresentstudy,SaeedW,AbdElRahmanSetal[52]demonstratedlowT3,T4andincreasedTSHamongdiabeticsubjects.Srinidhietal[53]alsodemonstrateddecreasedT3,T4andincreasedTSHintype2diabeticswithoutanycomplicationsandtype2diabeticswithnephropathywhencomparedtocontrols.Outof30diabeticsubjectsinvestigatedinthepresentstudy,atotalof33.3%diabeticpatientsshowedthyroiddysfunctionwith26.7%showing(8)hypothyroidismand6.7%(2)hyperthyroidism.Also,6.7%i.e.2outof30controlshadhypothyroidism.Theseobservationsshowahighincidenceofabnormalthyroidhormonelevelsindiabeticswhichisinaccordancewithstudiesof VibhaUetal.[54]PasupathiPetal[55] demonstratedthatoutof100diabeticpatientsstudied,28%hadlowplasmathyroidhormonelevels,17%hadhighthyroidhormone,and55%hadeuthyroidlevels.Thisstudyhasshownahighincidenceofabnormalthyroidhormonelevelsamongthediabetics.KashiZetal[56]inaComparativecross-sectionalstudydemonstratedtheprevalenceofHypothyroidismindiabeticsas17.5%.Proportionofhypothyroidismwas7.59%andhyperthyroidismwas2.31%,whiletheproportionoftotalthyroiddysfunctionwas9.9%amongdiabeticsaccordingtoImamsubektietal. [57]UppalVetal[58]inaCasecontrolstudydemonstratedprevalenceofhypothyroidismindiabetesmellituspatientsas17%.

DistillerLAetal[59]inaCross-sectionalstudydemonstratedprevalenceofhypothyroidismindiabetesmellituspatientsas11.8%.PalmaCCSSVetaldemonstratedprevalenceofSubclinicalhypothyroidism13%(type1diabetes)and12%(type2diabetes).[60]Inpresentstudy,Pearsoncorrelationtest,showsthattherewereresignificantpositivecorrelationsbetweenTSHandTC,LDL-CandTG,andnegativecorrelationsbetweenTSHandHDL-

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CofT2DMstudysubjects.Furthermore,thereweresignificantnegativecorrelationsbetweenT4&T3andTC,LDL-CandTG,andpositivecorrelationsbetweenT4&T3andHDL-CofT2DMstudysubjects.Thus,alowthyroidfunctionwaspositivelyassociatedwithalipiddysregulationinT2DMpatientsastherewasapositivesignificantrelationshipbetweenTSHandTG,LDL-CandTCinadditiontonegativesignificantcorrelationbetweenTSHandHDL-CamonghypothyroidT2DMstudysubjects.Hypothyroidismisassociatedwithmanybiochemicalabnormalities.Levelsoftotalcholesterolandlowdensitylipoproteincholesteroltendtoincreaseasthyroidfunctiondeclines.·Thushypothyroidismcausessecondarydyslipidemia.Inhypothyroidpatients,thereisoftenanincreaseintheserumtotalcholesterolconcentrationdespitethereducedactivityofHMGCoAreductasemainlyduetoraisedlevelsofserumLDLcholesterolandintermediatedensitylipoprotein(IDL)cholesterol.

Apositiveassociationbetweenoverthypothyroidismandhypercholesterolemiaiswellrecognized,butevidenceforsucharelationshipinsubclinicalthyroiddiseaseisinconsistent.Therelationshipbetweenserum TSHandcholesterolappearstobemodifiedbyinsulinresistanceineuthyroidnondiabeticadults,thosewithhigherserumTSHandrelativeinsulinresistanceareatgreatestriskofdyslipidemia. TherearesignificantindependentassociationsbetweenTSHandserumTC,HDL-C,andTGsaswellasthederivedparametersTC/HDL-Candnon-HDL-Cinrelativelyinsulin-resistanttype2patients.Jungfoundmeanplasmatotalcholesterol and LDLcholesterollevelselevatedinhypothyroidcasesthaninnormalcontrols.Meantotalcholesterol,LDLcholesterolandtriglyceridesw erefoundsignificantlyincreasedwhereasHDLcholesterolwasfoundsignificantlydecreasedincasesc omparedtocontrolsaccordingtoKhanMAH,Majumderetal[61]whichisinaccordancetothepresentstudy.

Thyroid dysfunction was seen in the current study in diabetic individuals with greater BMI, and TSH strongly linked with BMI. Obesity is thought to increase the risk of heart attacks and thyroid gland problems. Adult anthropometric parameters, such as waist circumference and body mass index (BMI), were found to have an inverse linear relationship with blood thyroid stimulating hormone (TSH) levels. TSH and free triiodothyronine (fT3) serum levels were greater in obese children than in non-obese children, and the TSH associated favourably with total cholesterol (TC), triglycerides (TG), and systolic blood pressure. Although previously explored, the relationship between the thyroid profile and body mass measurements such as BMI is not well understood. The majority of current research on this connection has produced contradictory findings.

Impact of hyperthyroidism on diabetesNumerous explanations have been offered to explain why hyperthyroidism causes hyperglycemia in clinical studies. In a thyrotoxic environment, insulin has a shorter half-life; this is assumed to be because the active hormone is degraded more quickly and inactive precursors are released. Additionally, it has been hypothesised that hyperthyroidism increases glucose synthesis by upregulating gluconeogenesis, which results from increased lipolysis and excessive lactate formation, as well as by increasing hepatic output by upregulating the GLUT2 glucose transporter's expression. These are made worse by

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increased glucose absorption in the digestive system. These processes may explain why diabetes patients with hyperthyroidism may have worsening blood glucose levels when their hyperthyroidism is not controlled.

Impact of hypothyroidism on diabetesControl of diabetes can also be impacted by hypothyroidism. Because the liver's diminished ability to produce glucose can lead to hypoglycaemic episodes, hypothyroidism may conceal the clinical manifestations of diabetes. This also explains why hypothyroid diabetes patients may need less insulin than those without thyroid illness. [3,22]

CONCLUSION

The current study was conducted at the Kakatiya Medical College MGM hospital in Warangal's Department of Biochemistry. The study involved 60 people: 30 T2DM patients without thyroid dysfunction served as cases, while 30 healthy non-diabetic people served as controls. FPG, serum TC, serum TAG, serum HDL-C, serum VLDL-C, serum LDL-C, serum T3, serum T4, and serum TSH, as well as BMI, were examined in both groups. In the current study, type 2 diabetics' blood T3 and T4 levels fell while their serum TSH levels rose when compared to controls. A substantial positive link between FBG and TSH and a negative correlation between FBG and the T3 and T4 of study participants with T2DM were found in the current investigation, according to the Pearson correlation test.

In type 2 diabetics, abnormal thyroid hormone levels are more common, with hypothyroidism being the most prevalent thyroid issue. Increased dyslipidemia in type-2 DM was linked to thyroid dysfunction (hypothyroidism). According to the current study's Pearson correlation test, there were substantial negative correlations between T3 and T4 and BMI of the study patients with T2DM and positive correlations between TSH and BMI.

According to anecdotal evidence, some T2DM patients are already routinely checked for thyroid illness. This may be reasonable in light of the information provided here and the relatively inexpensive nature of a blood TSH test. We are not aware of any official evaluations of this, though.

Future assessments of the scope of this practise, based on pertinent real-world facts and a cost-benefit analysis, may contribute to the justification for routine screening and, eventually, clear up this area of medical care.

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