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By SA Karim, J Samira, SMR Raihan, MS Emran, O Faroque, L Ali & H Mehtab

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SA Karim [1], J Samira [2], SMR Raihan [3], MS Emran [4], O Faroque [5], L Ali [6] & H Mehtab [7]

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Results: During the study, it was found that mean± SD of the thyroid hormone pictures in diabetic and control subjects of TT_3; (ngm/dl) {in controls (88.91±15.88) and in diabetic subjects (84.27±22.29)} was not statistically significant to each other (p=0.209). Mean±SD of TT_4 (µgm/ dl) in control subjects was 8.32±1.64 and in the diabetic subjects was 9.26±1.44, which is almost similar in both the groups (p= 0.589). FT4: (pgm/ml) in control subjects was 2.60±0.54 and in diabetics was 2.53±1.72 (p= 0.830). FT_4. (µgm/ dl) in control subjects was 1.43±0.22 and in diabetics subjects 1.36±0.25. (p 0.179). TSH (µlu/ml) in control subjects was 1.34±1.00 and in diabetic subjects 1.54±1.21 (p: 0.411). FT_3; FT_4 and TSH showed no significant difference between control and diabetic subjects. Thyroid hormones (TT_3, TT_4, FT_3, FT_4) and TSH were reanalyzed according to HbA1c and BMI category and showed no significant differences. But when the FPG and HbA1c goes beyond 12 mmol/l and 10% respectively there was more worsening thyroid hormone pictures in comparison to groups whose FPG and HbA1c were below 12mmol/l and 10%. It was also noticed there was a tendency to develop more lower thyroid hormone pictures and more deteriorating glycemic status in patient with low and normal BMI groups in comparison to higher BMI groups of patients.

Conclusion: Uncontrolled type2 diabetes mellitus is associated with alteration of thyroid hormone pictures particularly affecting TT_3, FT_3 and TSH in absence of clinically evident thyroid diseases. This biochemical feature is more evident if the BMI of the Diabetic subjects is low or within the normal range and also the more worsening the glycemic status as determined by FPG and HbA1c, there was more deteriorating circulating serum thyroid hormone pictures.

Keywords: euthyroid sick syndrome (ESS), diabetes mellitus, body mass index (BMI).

I. Introduction

Diabetes mellitus (DM) is one of the important health problems affecting the major population worldwide. Diabetes mellitus is an endocrine disorder which involves multiple organ systems and leads to significant morbidity and mortality due to accompanying complications.[1.] Diabetes mellitus is characterized by absolute or relative deficiency in insulin secretion or insulin action or both, associated with hyperglycemia and disturbances in carbohydrate, lipid and protein metabolism.[2]

Thyroid diseases and diabetes mellitus are the two most common endocrine disorders[3]. Diabetic patients have increased prevalence of thyroid disorder, with hypothyroidism being the most common.[4] In diabetic patients, thyroid dysfunction varies from 2.2% -17%.

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Diabetic women are more commonly affected than men.[5] Hypothyroidism is a clinical syndrome occurs from a deficiency of thyroid hormones. It is very common thyroid problem in diabetic patients.[6] Thyroid hormones and insulin are the antagonistic, and involved in the metabolism of carbohydrates, proteins, and lipids. Thyroid hormone as well as insulin levels are altered if there is functional impairment of the thyroid gland and endocrine pancreatic beta cells.[7] Thyroid disorders adversely affect diabetes control. Diabetes Mellitus appears to influence thyroid function in two sites; firstly, at the level of hypothalamic control of TSH release and secondly at the conversion of T_4 to T_3 in the peripheral tissue. Increased hyperglycemia causes reversible reduction of the activity and hepatic concentration of T_4-5'-deiodinase, low serum T_3, increase in reverse T_3 and also variation in the level of T_4.[8]

Euthyroid Sick syndrome (ESS) or Non-thyroidal illness Syndrome (NTIS) identifies abnormalities of thyroid function tests observed in patients with systemic non-thyroidal illnesses and in those patients undergoing surgery or fasting.[9-11] Abnormalities of thyroid function tests observed in ESS or NTIS includes 1) Low T_3 Syndrome 2) Low T_3 and T_4 syndrome 3) High TT_4 syndrome 4) other abnormalities like low TT_3 and TSH, high TSH and low TT_3 and TT_4.[12]

Experiments on both animal and human models Diabetes Mellitus was found to be associated with alteration of thyroid hormone picture in absence of clinical thyroid diseases irrespective of the type of diabetes. In both type1 and type2 diabetes significant reduction of both TT_3 and FT_3, increased rT_3 and high rT_3/T_3 ratio was demonstrated.[13-16] Serum FT_4 and FT_4I were normal, TT_4 was normal or suppressed and TSH was found normal or slightly elevated.[17, 18] All the parameters of thyroid function specially TT_3, FT_3 and rT_3 become normal when euglycemia was achived.[14,19,20] More over it was found that reduction of FT_3 and TT_3, rise of rT_3 are significantly correlated with the severity of hyperglycemia and the thyroid secretory response to large dose of TSH is also declined in uncontrolled diabetes mellitus which frequently improves with improved glycemic control.[21]

A previous study among young Bangladeshi diabetic population demonstrated significant alteration of thyroid hormone pictures in absence of clinical thyroid diseases which is consistent with the other study done in abroad earlier.[22] But ESS or NTIS in the setting of type2 diabetes was not investigated extensively earlier and there is no available data regarding the changes in thyroid hormone pictures in patients with uncontrolled type2 Diabetes Mellitus among Bangladeshi population. Although there are few studies in abroad; which revealed that that there are significant alteration of thyroid hormones in uncontrolled type2 diabetic subjects.[19,20,23,24] As most of these studies did not exclude other causes of ESS or NTIS which are responsible for activating inner ring deiodination or inhibition of outer ring deiodination of T_4 to produce T_3 from T_4 instead of rT_3;[25] the result was found to be poorly representative.

In the above context our present study was designed to document the changes of thyroid hormones pictures in absence of clinical thyroid diseases among Bangladeshi population in the setting of uncontrolled type2 diabetes mellitus.

II. Objectives and Methods

To evaluate the circulating thyroid hormone pictures in absence of clinical thyroid diseases among type 2 diabetic subjects in a group of Bangladeshi population.

III. Methodology

a) Types of study

This was a case and control study.

b) Place and duration of study

The study was conducted in the Endocrinology department of Sylhet MAG Osmani Medical College (SOMC) and Hospital, Sylhet, Bangladesh in collaboration with the Research Division, BIRDEM, Dhaka, Bangladesh during the period of January 2016 to December 2017.

c) Study population

A total of 100 type 2 diabetic subjects, 30-50 years of age, irrespective of glycemic status, duration of diabetes, BMI and sex were recruited from the outpatient department (OPD) of SOMC hospital and BIRDEM hospital. Prior to recruitment, diabetes mellitus was confirmed according to current American Diabetic Association (ADA) criteria for the diagnosis and classification of diabetes mellitus.[24] Control subjects (n=100) were selected from friends and family of the patients within 5 years of age band without diabetes or impaired glucose regulation (IFG, IGT) determined according to ADA criteria[24] and having no clinical thyroid diseases or other evident systemic diseases documented on clinical evaluation. Informed written consent was taken from all recruited diabetic and control subjects for the purpose of the study.

d) Exclusion criteria

- Type 2 diabetes with acute metabolic de-compensation.
- Type 2 diabetes with clinically detectable thyroid diseases.
- Type 2 Diabetes with clinically diagnosed other acute or chronic systemic diseases.
- Diabetic subjects with overt nephropathy in which serum creatinine > 2mg/dl
- Pregnancy and postmenopausal woman.

e) Method

Selection criteria as per availability and was given an appointment to come in a particular date. Preparation of the subjects and collection of blood of the Controls and diabetic subjects that were assigned for the purpose of study done according to the recommendation of the "Report of the Expert committee of the Diagnosis and Classification of Diabetes Mellitus.[24] They were requested to fast overnight for at least eight hours and in the subsequent morning 16 ml of venous blood was drawn from the ante-cubital vein by using 25 cc disposable plastic syringe with 18G needle for the estimation of fasting serum insulin, C-peptide, glucose, HbAlc, TT_3, TT_4, FT_3, FT_4 and TSH. One ml of collected venous blood was taken in an anticoagulant containing vial for estimation of HbAlc. Remaining 15ml of blood was kept in 3 separate plain test tubes in equal amounts (5ml in each) to centrifuge immediately. Blood sample contained in the test tube was centrifuged for 15 minutes at a rate of 4000 rpm. A total of 200 μl of serum was collected in appropriately labeled eppendorf in duplicate with the help of micropipette for each of the biochemical parameters. Then the serum sample was preserved immediately at -30° C for analysis.

f) History and clinical examination

Detailed socio-demographic and clinical data were recorded in a pre-designed case record form. These include age, sex, residing area, occupation, socioeconomic status, dietary habit, exercise, alcohol and smoking habit, duration of diabetes, associated diseases like hypertension, obesity, dyslipidemia, coronary artery disease, cerebrovascular diseases, peripheral vascular diseases and crystal deposition diseases. Family history of these diseases were also been noted. Classical and non-classical features of diabetes mellitus and any adverse outcome of diabetes on life style was noted by taking history from the diabetic subjects.

Hight, weight, BMI, waist circumference, hip circumference, waist hip ratio (WHR), waist height ratio (WHtR) of all the controls and diabetic subjects were recorded. Percent body fat and total fat mass was measured by "Body logic Body fat monitor; Omron Corporation, Japan". Systolic and diastolic blood pressure of all patients and control subjects was recorded. Blood pressure was measured by using mercury sphygmomanometer after at least 5 minutes of recumbence in a calm and quiet environment. Systolic blood pressure 130 mm Hg and the diastolic blood pressure 85 mm Hg was taken as the cut-off value for categorizing the normal and the abnormal values among diabetic population.[25] Diabetic neuropathy was tested by appropriate clinical test. Autonomic function test were done by documenting the heart rate variability and blood pressure response on standing. Motor neuropathy was tested by eliciting jerks and reflexes by the percussion hammer. Retinopathy of all diabetic subjects was screened by routine dilated fundoscopy of the BIRDEM opthalmology outpatient department and SOMC hospital outpatient department. For the documentation of nephropathy, urine albumin in mg/l and urine creatinine in g/l was estimated to calculate the albumin creatinine ratio (ACR). FPG was measured by glucose oxidase method and HbA1c wes measured by HPLC based analyzer, Insulin, c-peptide, TT3, TT4, FT3, FT4 and TSH was measured by Chemiluminescence technique in Immulite Auto-analyzer.

g) Statistical analysis

All the data were expressed as mean standard deviation, median (range) and/or number and percentage (%) as appropriate. Statistical analysis was done by using SPSS 7.5 packages for windows. Appropriate statistical test of significance like unpaired t test, one way analysis of variance (ANOVA) and Mann-Whitney test was used as necessary. $P < 0.05$ was taken as minimum level of significance.

h) Data presentation

Tabulation and / or drawing either in the form of graph or in the form of diagram were utilized as necessary for data presentation.

IV. Results

Table-1: Demographic status of the study group

Groups	Age mean ± SD	Annual Income Median (Range)	Family Member	SBP mean ± SD	DBP mean ± SD	Duration of DM, years
Controls (n =30)100	39.53± 5.24	120000 (30000-220000)	6 ±1	120 ±23	80±7	--
DM(n=100)	39.24± 5.79	100000 (20000-200000)	6± 2	124 ±17	80±10	0.02 (0.01- 6)
t/p value		u/p value	t/p value			
Cont vs DM	-.248/0.804	1114/0.32*	1.1770/.241	1.177/0.241	1.101/0.273	--

In table-1 shows demographic status of the study group where mean±SD age of the control and diabetic subjects were 39.5±5.2 and 39.2±5.8 respectively. Duration of diabetes is one month to six years. Systolic and diastolic blood pressure of the control and diabetic subjects were almost similar and it was within normal range. The table given below showed it in detail:

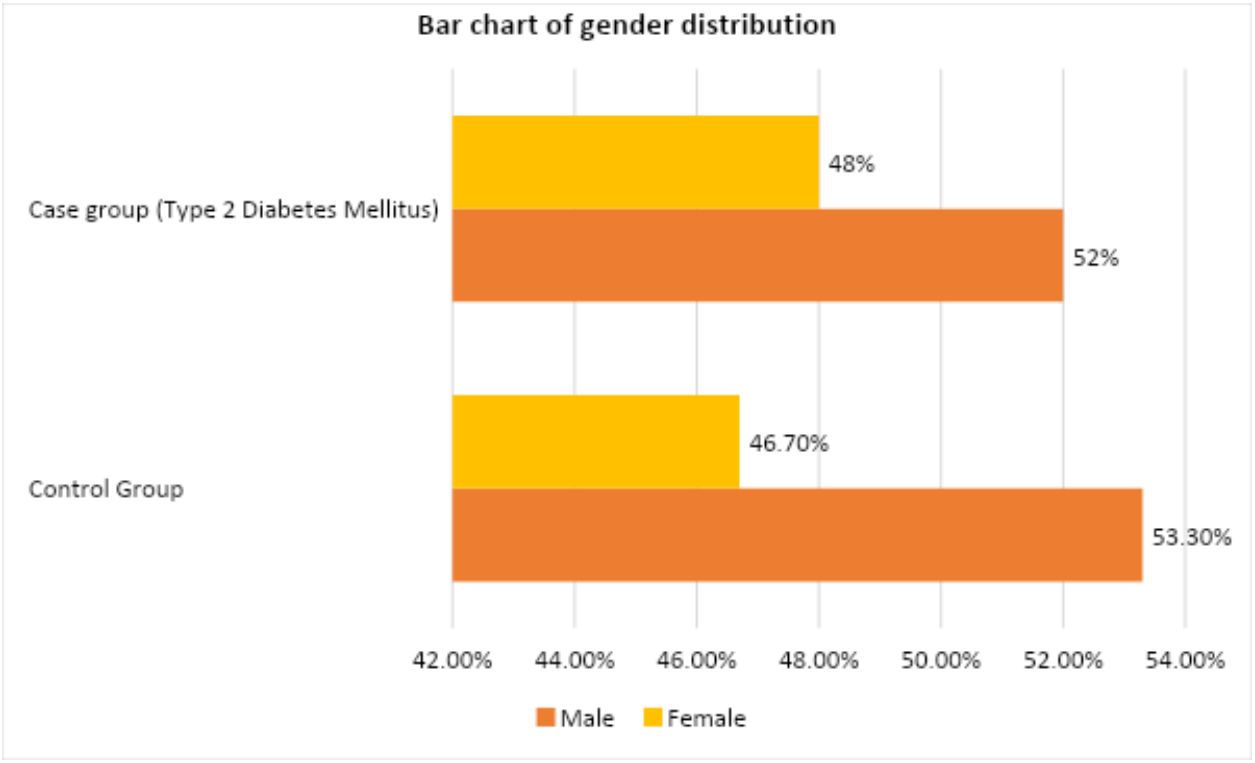

Figure-1: Gender distribution of the study group.

In figure-1 shows gender distribution of the study group where both the groups have shown in the figures in details. Male persons are 53/3% and females are 46.7% in controls and in type Diabetic group male patients are 52% and females are 48%.

Table-2: Clinical status of the study group

Clinical history		Controls		Type-2 Diabetes mellitus	
		Number	Percentage	Number	Percentage
Sex	Male	53	53	52	52
	female	47	47	48	48
Type of work	Sedentary	90	90	84	84
	Physical work	10	10	16	16
Exercise	Regular	37	37	23	23
	Irregular	63	63	57	57
	No Exercise	0	0	20	20
Smoking	Smoker	7	7	20	20
	Non Smoker	90	90	70	70
	Past Smoker	3	3	10	10
FH diabetes	Present	53	53	65	65
	Absent	47	47	23	23
FH HTN	Present	50	50	48	48
	Absent	50	50	36	36
FH obesity	Present	44	44	46	46
	Absent	56	56	54	54
FH CAD	Present	27	27	24	24
	Absent	73	73	52	52
FH CVD	Present	24	24	27	27
	Absent	76	76	50	50
H/O CAD	Present	4	4	38	38

H/O CVD	Present	0	0	06	6
Retinopathy	Present	0	0	35	35
Neuropathy	Present	0	0	35	35
Nephropathy	Present	0	0	25	25
Anti DM drugs	Present	0	0	24	24
Typical Symptoms	Present	0	0	37	37
Atypical Symptoms	Present	0	0	63	63

In table-2 shows clinical status of the study group where 53 out of 100 controls and 65 out of 100 diabetics have family history of diabetes. Family history of hypertension was found in 50 out of 100 and 48 out of 100 controls and diabetic subjects respectively. Family history of obesity was found in 44% controls and 46% diabetic subjects. Around 27% of controls and 24% of diabetic subjects have family history of coronary artery diseases (CAD) and 24% of control and 27% of diabetic patients have family history of cerebrovascular diseases (CVD). Early retinopathy and neuropathy were observed in 45.5% and 36.5% diabetic subjects. Nephropathy was documented in 25 diabetic subjects.

Table-3: Thyroid hormone status in diabetic and control subjects

Parameters	Control			DM			P value			
	MC**	FC**	TC**	MD**	FD**	TD**	MCvs MD	FC vs FD	TC vs TD	MD vs FD
TT_3	93.67± 17.14	83.46 ±12.78	88.91 ±15.88	85.02 ±22.7	83.46 ±22.0	84.27 ±22.3	0.912	1.00	-1.268 /0.209	1.00
TT_4	8.54± 1.9	8.07± 1.31	8.32 ±1.64	8.22 ±1.90	8.63 ±1.69	9.26 ±9.44	1.00	1.00	0.54/ 0.589	1.00
FT_3	2.69 ±0.36	2.56 ±0.55	2.60 ±0.54	2.40 ±0.68	2.37 ±0.74	2.53 ±1.72	0.816	1.00	0.215/ 0.83	1.00
FT_4	1.49 ±0.21	1.37 ±0.23	1.43± 0.22	1.43 ±0.18	1.31 ±0.27	1.36 ±0.25	1.00	1.00	-1.35/ 0.179	0.065
TSH	1.33 ± 0.88	1.35 ±1.16	1.34 ±1.00	1.26 ±0.89	1.84 ±1.42	1.54 ±1.21	1.00	0.961	0.824/ 0.411	0.08

***(MC=Male control, FC= Female Control, TC= Total Control, MD=Male Diabetic, FD= Female Diabetic, TD=Total Diabetic)*

In table-3 shows thyroid hormone status in diabetic and control subjects. Mean±SD of TT3; (ngm/dl) in controls (88.91±15.88) and in diabetic subjects (84.27±22.29) was not statistically significant to each other (p=0.209). Mean±SD of TT4 (μgm/dl) in control subjects was 8.32±1.64 and in the diabetic subjects was 9.26±1.44, which is almost similar in both groups (p= 0.589). FT3 (pgm/ml) in control subjects was 2.60±0.54 and in diabetics was 2.534±1.72 (p= 0.830). FT4 (ngm dl) in control subjects was 1.43±0.22 and in diabetics subjects 1.36±0.25. (p 0.179). TSH (μlu/ml) in control subjects was 1.34±1.00 and in diabetic subjects 1.54±1.21. (p: 0.411). FT3; FT4 and TSH showed no significant difference between control and diabetic subjects.

Table 4: Mean serum level of TT3, FT3 and TSH in patients with low levels of hormones and also in patients with normal values of hormones

Groups	TT3	FT3	TSH
Groups with Low level of Thyroid hormone	58.46±12.32	1.31±0.44	0.50±0.49
Groups with Normal level of Thyroid hormone	93.81±16.91	2.53±0.59	1.50±0.86
T/p value	-11.45/0.0001	-6.83/0.0001	-6.018/0.0001

(Results are expressed as mean±SD, p value was calculated using ANOVA Bonferrony, t/p value was calculated using unpaired 't' test)

Table-4 showed that the mean serum TT3 in patients with low T3 syndrome groups of patients and in patients with normal values of TT3 were 58.46±12.32 and 93.81±16.91 respectively which was statistically significant (p=0.0001) between the two groups. Mean Serum TSH level in low TSH group was 0.47±0.395 and in normal TSH group was 1.50±0.86 which was statistically different significantly (p=0.0001) from each other. Serum FT3 levels in low FT3 groups and normal FT3 groups of patients were 1.31±0.44 and 2.53±0.59 respectively which was statistically different between the two groups.

Table-5: Thyroid hormone pictures in diabetic subjects according to HbA1c

Groups	TT_3	TT_4	FT_3	FT_4	TSH	FPG	HbA1c	S Insulin	Serum C-Peptide
Group A, N=13	78.42± 24.50	8.77± 1.15	2.40 ±0.59	1.37± 0.25	1.37± 0.25	5.97± 1.8	6± 0.56	5.9 (3.5-12.5)	0.88 (0.11-5.1)
Group B, N=15	89.71± 24.33	8.00 ± 1.53	2.35± 0.61	1.22± 0.27	1.90± 1.40	7.7± 1.9	7.37± 0.32	8.0 (3.2-16.3)	0.71 (0.12-2.1)
Group C, n=72	84.19 ±21.51	8.45 ±1.95	2.35± 0.73	1.39± 0.24	1.41± 1.11	12.39± 4.5	10.84± 1.89	7.9 (19-48.9)	0.74 (0.06-3.6)
P value								U/p value	
A vs B	0.554	0.773	0.255	0.774	0.135	0.749	0.09	75/0.30	88.5/0.67
A vs C	1.000	1.000	1.000	1.000	1.000	0.000	0.000	343/0.13	392/0.35
B vs C	1.000	1.000	1.000	0.97	0.862	0.000	0.000	513/0.76	469/0.42

(Group A=HbA1c < 7%, Group B=HbA1c 7%-8%, Group C=HbA1c > 8%)

(P value was calculated using one way analysis of variance, U/p value was calculated using Non-parametric Mann Whitney U test.)

In table-5 shows thyroid hormone pictures in diabetic subjects according to HbA1c. Thyroid hormones (TT_3, TT_4, FT_3, FT_4) and TSH were analyzed according to HbA1c category and showed no significant difference.

Table 6: Thyroid hormone pictures among Diabetic subjects when categorized according to BMI

Groups	Serum Insulin	Serum C peptide	FPG mg/dl	HbA1c%	TT_3	TT_4	FT_3	FT_4	TSH
BMI A N=55	6.0 (1.9-38.0)	0.74(0.06-3.62)	11.77±5.18	10.35±2.63	81.45 ±20.70	8.51± 1.77	2.31± 0.68	1.41± 0.26	1.28 ±0.89
BMI B N=35	8.6 (2.3-48.9)	0.76(0.12-5.11)	9.66±3.79	8.83±2.01	89.54± 24.58	8.46± 1.78	3.02± 2.72	1.32± 0.26	1.78 ±1.51
BMI C N=10	14.9 (4.9-21.5)	0.94(0.20-2.13)	9.96±3.30	9.10±2.01	81.33± 20.62	7.74± 2.15	2.00± 0.56	1.29± 0.18	2.09 ±1.30
u/p value		P Value							
A Vs B	710/0.036	811/0.21	0.108	.013	0.285	1.000	0.164	0.721	0.160
A vs C	140/0.014	219/0.30	0.761	.399	1.000	1.000	1.000	0.651	1.000
B vs C	120/0.13	172/0.93	1.000	1000	0.913	1.000	0.288	1.000	1.000

(BMI A=BMI upto 25). (BMI B=BMI 25.1-30). (BMI C=BMI>30)

(P value was calculated by ANOVA Bonferrony, U/p value was calculated using Mann-Whitney U test)

Table-6 showed that when TT_3 , TT_4, FT_3, FT_4 and TSH were grouped according to BMI category and compared separately among control and Diabetic subjects in three BMI groups; no significant difference was observed.

Table 7: Glycemic Status and indices of obesity in patients with low T_3 syndrome and in patients with having normal T_3 among the Diabetic subjects categorized according to BMI groups

Groups		FPG	HbA1c	BMI	% body Fat	Total Fat Mass	Fasting Serum Insulin	
BMI A	Low T_3	14.24±7.13	10.74±3.15	23.16±1.39	23.46±5.45	7.6 (1.92-18.3)	7.6 (1.92-18.3)	
	Normal T_3	1018±3.61	10.18±2.39	22.74±1.89	25.48±5.84	5.55 (1.9-38.0)	5.55 (1.9-38.0)	
	t/p value	1.96/0.064	0.721/0.474	0.813/0.420	-1.210/0.23	u/p value	u/p value	*281/0.44
BMI B	Low T_3	9.55±4.40	9.08/±2.41	27.19±1.25	33.31±4.83	8.0 (2.3-47)	8.0 (2.3-47)	
	Normal T3	9.70±3.68	8.76±1.93	27.33±1.45	3.72±5.82	8.8 (3.5-48.9)	8.8 (3.5-48.9)	
	t/p value	-.094/0.925	0.380/0.706	-0.233/0.817	1.146/0.26	u/p value	u/p value	*99/0.72
BMI C	Low T_3	10.45±0.64	9.55±1.34	33.41±3.61	36.85±6.29	13.4 (5.3-21.5)	13.4 (5.3-21.5)	
	Normal T_3	9.84±3.73	8.99±2.54	31.63±1.60	37.30±4.10	14.9 (4.9-20.8)	14.9 (4.9-20.8)	
	t/p value	0.222/0.83	0.294/0.776	1.144/0.286	-.182/0.901	0.335/0.726	u/p value	*7.0/0.79

(BMI A=BMI upto 25). (BMI B=BMI 25.1-30). (BMI C=BMI>30)

Table-7 showed that when diabetic patients with low T_3 and Normal T_3 were reanalyzed according to BMI category then it was found that low T_3 subjects having normal BMI showed significantly higher serum fasting glucose (14.24±7.13) levels compared to the patients with normal T_3 (10.66±3.61).

Table 8: Glycemic status, % body fat and total fat mass in different status of thyroid hormones

Groups		FPG	HbA1c	Fasting S. Insulin	BMI	%Body Fat	Total Fat Mass
TT_3	LowTT_3 (n=27)	12.57±6.44	10.16±2.89	7.7(1.9-47.0)	25.11±3.35	27.37±3.74	18.12±5.93
	Normal TT_3 (n=73)	10.21±3.63	9.52±2.32	8(1.9-48.9)	25.41±3.45	28.72±6.83	19.14±6.13
	t/p value	2.30/0.024	1.572/0.119	972/0.92*	-0.384/0.702	-0.856/0.394	-0.753/0.453
FT_3	LowFT_3 (n=12)	11.45±5.09	9.98±2.43	7.4(4.4-38.0)	26.59±3.52	30.42±7.24	21.42±5.94
	Normal FT_3 (n=88)	10.77±4,61	9.66±2.51	7.8(1.9-48.9)	25.16±3.33	28.07±6.91	18.52±6.03
	t/p value	0.475/0.636	0.426/0.671	480.5/0.61*	1.357/0.178	1.096/0.276	1.562/0.122
TSH	Low TSH (n=12)	12.24±4.16	10.86±2.48	8.3(1.9-48.9)	25.27±1.82	30.19±7.65	19.98±5.0
	Normal TSH (n=88)	10.81±4.78	9.65±2.48	7.7(1.96-47.0)	25.21±3.65	27.63±6.66	18.40±6.20
	t/p value	0.986/0.327	1.573/0.137	461.5/0.48*	0.449/0.218	1.524/0.782	0.982/0.624

Table-8 showed the analysis of TT_3, FT_3 and TSH and its relationship to FPG, HbA1c, Fasting serum insulin, BMI and also with %body fat and total fat mass. 27 diabetic subjects have shown T_3 levels below the lower limit of normal range at FPG levels12.57±6.44 and HbA1c 10.16±2.89. FPG value was significantly (p=0.024) higher in low T_3 group compared to normal TT3 group. 12 diabetic subjects were found to have FT_3 below the lower limit of normal range at FPG level 11.45±5.09 and HbA1c level 9.98±2.43. Again 12 diabetic subject were found to have TSH below the lower limit of normal range at FPG level 12.24±4.16 and HbA1c level 10.86±2. Fasting serum insulin levels showed no significant differences among the different groups of TT_3, FT_3 and TSH. Similar observation was also noted in case of %body fat, total fat mass and in BMI.

Figure 2 and Figure 3

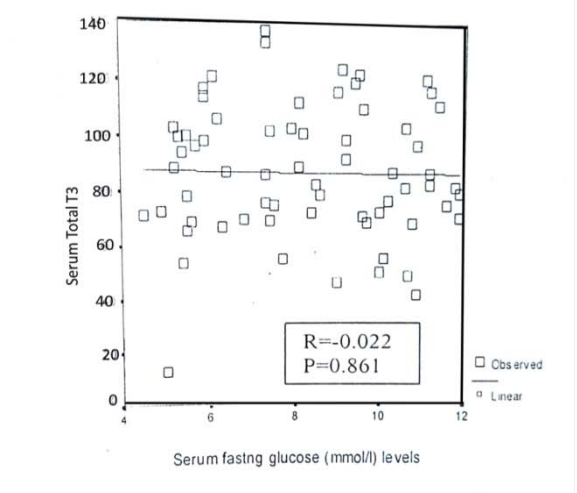

Figure 2: Relationship of FPG with Serum TT3 of the Diabetic Subjects when FPG <12mmol/l

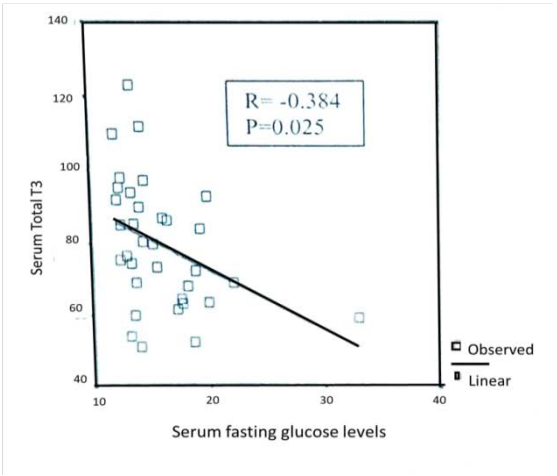

Figure 3: Relationship of FPG with Serum TT3 of the Diabetic subjects when FPG>12mmol/l

V. Discussion

Some studies done earlier in abroad; the age (mean±SD) of type 2 diabetic patients who were participated in study was (47.5±7.4) years coincides with the fact that type 2 diabetes mellitus usually develops after the age 40 years.[9, 26,27]. Where as in our study age (mean±SD) of the control and diabetic subjects were 39.5±5.2 and 39.2±5.8 respectively.

Thyroid hormones among control and Diabetic subjects was evaluated and it was found that the differences observed in serum thyroid hormones and TSH levels between controls and diabetic subjects were not statistically significant. When the thyroid hormones and TSH were reevaluated on the basis of BMI and HbAlc groups among the diabetic subjects, similar observation was noted (table 5 and 6). But when serum TT_3, TT_4, FT_3, FT_4, and TSH values of all the diabetic subjects were divided into two groups by applying the cut off values to each hormone into normal values of thyroid hormones group and TSH with low values of thyroid hormones groups and TSH among the diabetic subjects, 27 diabetic patients were found to have low TT_3 below the lower limit of normal range than that of their normal counterpart which was significant at p=0.0001 level (table-4 and 8), 12 patients were found to have serum

FT_3 levels which was significantly (p=0.0001) lower than their normal counterpart groups. Again 12 diabetic subjects were found to have low TSH level than their normal groups. 4 diabetic subjects were found to have significantly lower serumTT_4 when compare to normal TT_4 groups. When the TT_3. FT_3, TT_4, and TSH groups were reanalyzed in relation to fasting serum glucose and HbA1c, low thyroid hormones and low TSH group have significantly (p=0.0001) higher fasting serum glucose and HbA1c than the groups with hormones within the normal range(table-8). The diabetic patients with Low TT_3 showed strong negative correlation to FPG and HbA1c (Fig: 19, 20). This finding is consistent with the findings of the other studies done in abroad in both type 1 and type 2 diabetic subjects.[11-16,28-31]. Our findings showed that around the level of 12mmoll of fasting serum glucose was associated with marked alteration of thyroid hormone picture in the blood in absence of clinical thyroid diseases. When low TT_3 group was categorized according to BMI, diabetic subjects having BMI within normal range was found to have more deteriorating fasting serum glucose, HbA1c and serum TT_3 levels; compare to other BMI groups (Table-8). This finding suggests that changes in thyroid hormone possibly much more obvious in young diabetic groups who are mostly have low or normal BMI than the type2 diabetic subjects that are mostly associated with obesity and higher degrees of BMI. These findings also supports the findings of the others study done in abroad.[21] and also in the cell and molecular biology department of BIRDEM, Dhaka, Bangladesh.[22] Our findings also conclude that BMI and other indices of obesity possibly have very little or no impact on serum thyroid hormones and TSH levels until and unless they are associated with very high serum fasting glucose levels beyond 12mmol/l.

VI. Conclusion

1. Uncontrolled type 2 diabetes mellitus is associated with alteration of thyroid hormone pictures particularly altering the TT_3, FT_3 and TSH in absence of clinically evident thyroid diseases.
2. This biochemical feature is more evident if the BMI of the subjects is low or normal range and it was also found that the more worsening the glycemic status as determined by FPG and HbA1c, there was more deteriorating circulating serum thyroid hormone pictures and TSH.
3. Interpretation of abnormal thyroid hormone pictures requires a very high index suspicion in patients with uncontrolled type2 diabetes mellitus as it was found to have associated with ESS or NTIS.

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