Research Paper

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Frequency and Relevance of Thyroid Dysfunction In Patients With Type II Diabetes Mellitus

Medical Science

KEYWORDS : type 2 diabetes mellitus, hyperthyroidism, hypothyroidism

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ABSTRACT

Objectives : The purpose of the study was to evaluate the profile of thyroid dysfunction in type 2 diabetics. The study aims to find the dysfunction most prevalent i.e. subclinical hypothyroidism, hypothyroidism, hyperthyroidism or subclinical hyperthyroidism and to find the relative frequency of each group.

Background : Diabetes often coexists with other medical disorders like obesity, hypertension, dyslipidemia, thyroid dysfunction. While the relation between Type 1 diabetes mellitus is proven beyond doubt, the relation between type 2 diabetes and thyroid dysfunction is still not very clear.

Methods : The diagnosis of diabetes was made as per ADA guidelines using random sugar, fasting sugar and post prandial sugar values. Thyroid function was evaluated by withdrawing venous blood sample and checking free T4 and TSH values. The total duration of the study was 20 months. The results were entered in a pre-determined proforma. Obtained data was statistically evaluated and conclusions were drawn at the end of the study.

Results : A total of 300 cases were evaluated during the study. 187 out of 300(62.33%) patients were male and 113 out of 300 (37.67%) patients were female. The mean age of the population was 58.32 with a SD of 8.64 years.

Conclusion : Our study indicates occurrence of thyroid dysfunction among type 2 diabetics(12.33% of diabetics had thyroid dysfunction), more in females. Subclinical hypothyroidism was the most common type of dysfunction in both sexes. Thyroid dysfunction was not significantly correlated with duration of diabetes, blood sugar levels, BMI of the patients.

INTRODUCTION :

Diabetes mellitus is a metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both; posing an enormous health problem in the country. The thyroid hormones play a critical role in cell differentiation during development and help maintain thermo genic and metabolic homeostasis in the adult. Both diabetes and thyroid disorders may have an insidious onset. Studies have shown thyroid dysfunction may increase the risk of atherosclerosis, dyslipidemias and cardiac problems in diabetes. Hence the purpose of the study is to evaluate the profile of thyroid dysfunction in type 2 diabetics with the aim being to improve patient care.

MATERIAL AND METHODS

Study design : Randomized and Prospective study in which a total of 300 patients were enrolled in accordance with the ethical standard of the institution and with the HELSINKI declaration of 1975, as revised in 2000. Approval of the institutional ethical committee was taken at the beginning of the study. Well informed written consent was taken from all participants.

Inclusion Criteria:

- Type 2 Diabetics were included in the study.
- Both males and females were included
- Both OPD patients as well as patients admitted to the ward were admitted in the study.

Exclusion Criteria:

Following group of patients were excluded from the study.

- Patients with known history of thyroid disorders prior to diagnosis of diabetes.
- Those having undergone thyroid surgery.
- Pregnancy.
- Type 1 Diabetes Mellitus.
- Critically ill patients.

Patients with chronic renal failure.

Patients taking medication that affect protein binding of the hormone as well as the synthesis and release of the hormone.

Statistical analysis : Various statistical tests were used for the analysis of data in the present study. These are given as following:

Arithmetic mean : It gives the average value of whole range of data given. It is given by the following

formula:

$$\bar{X} = \frac{\sum X}{N}$$

Where $\bar{X}$ = Arithmetic Mean

$\sum X$ = Sum of all variables

N = Total number of all Variables

Standard Deviations : It gives the degree of deviation of the recorded data from the mean. It is calculated by the following formula:

$$SD = \sqrt{\frac{\sum(X-\bar{X})^2}{N}}$$

Where SD= Standard Deviation

X= Individual Variables

$\bar{X}$= Mean of Variables

Chi-square Test : Several proportions can be compared using a 2 by k chi-square test. This is a test of the independence of the row and column variables, it is equivalent to the chi-square independence tests for 2 by 2 and r by c chi-square tables.

$$\chi^2 = \sum_{i=1}^{r}\sum_{j=1}^{c}\frac{(O_{ij} - E_{ij})^2}{E_{ij}}$$

where, for r rows and c columns of n observations, O is an observed frequency and E is an estimated expected frequency. The expected frequency for any cell is estimated as the row total times the column total then divided by the grand total (n).

RESULTS :

A total of 300 cases were evaluated during the study. 187 out of 300(62.33%) patients were male and 113 out of 300 (37.67%) patients were female. The mean age of the population was 58.32 with a SD of 8.64 years.

List of graphs attached

Graph No.1	Age and Sex distribution of study population	Refer Image 1
Graph No.2	Percentage of cases with deranged thyroid profile	Refer Image 2
Graph No.3	Distribution of patients in the study	Refer Image 3
Graph No.4	Distribution of thyroid dysfunction	Refer Image 4
Graph No.5A	Age wise distribution of patients with abnormal thyroid profile	Refer Image 5A
Graph No.5B	Mean Age of the patients with thyroid dysfunction	Refer Image 5B
Graph No.6	Abnormal Thyroid Dysfunction in Male Population	Refer Image 6
Graph No.7	Abnormal Thyroid Dysfunction in Female Population	Refer Image 7
Graph No.8	Duration of Diabetes in Patients with Thyroid Dysfunction	Refer Image 8
Graph No.9A	Distribution of thyroid dysfunction as per BMI	Refer Image 9A
Graph No.9B	Mean BMI of patients with thyroid dysfunction	Refer Image 9B
Graph No.10	Mean parameters of different classes	Refer Image 10

Table 1 : Mean parameters of different classes (Refer Graph No.10)

	Euthyroid	Subclinical hypo thyroidism	Clinical hypo Thyroidism	Subclinical hyper thyroidism	Clinical hyper Thyroidism	p-value
Sample size	263	24	7	4	2	-
BSL F	126.71	126.41	131.42	130.25	145.00	0.89 NS,p>0.05
BSL PP	175.79	180.12	179.57	187.25	163.50	0.81 NS,p>0.05
TSH	1.29	7.79	8.04	0.20	0.09	0.00 S,p<0.05
F T4	1.28	1.19	0.24	1.43	3.81	0.00 S,<0.05

DISCUSSION :

The relation between type 2 Diabetes Mellitus and thyroid dysfunction is not very clear. Any disorder that is even remotely linked with a disease of the magnitude of Type 2 Diabetes Mellitus should be investigated further. Few studies have been done with varying results on the type of thyroid dysfunction in type 2 Diabetes Mellitus. However the results have been inconsistent so far and a general consensus has not evolved regarding the same.

Total of 300 cases of Type 2 Diabetes Mellitus were selected and taken up for the study. The study sample of 300 patients consisted of 187 Males (62.33%) and 113 Females (37.67%). The mean age of the male population was 58.56 years with SD of 9.04 years and the mean age of the female population was 57.91 years with a SD of 7.96 years. The mean age of the entire study population was 58.32 years with a SD of 8.64 years.

Both prospective and retrospective analysis studies have been done to evaluate the thyroid dysfunction in type 2 DM.

The association between DM and thyroid disease has been recognized, though the reported prevalence of thyroid dysfunction in diabetic populations varies widely between studies.

The percentage of cases with deranged thyroid profile in the present study was 12.33%.this was comparable with Rajan SKet al[40] (15%), Nobre EL et al[37] (12.7 %) and Radaideh AR et al[38] (12.5%), Akbar DH et al[61] (16%), Perros P et al[62] (13.4%) and Aksar RA et al[65] at 12.9 %. The percentage as reported by Bal BS et al[39] was higher at 40 %(78/184) with autoimmune thyroiditis present in 32 cases. The percentage of patients was also higher in a study by Udiong CEJ et al[59] (46.5%) but this study also included type 1 DM patients, which could explain the higher number of cases. Higher figures were also published in two independent studies by Ramaswamy et al[41] (27%) and Kiran Babu et al[5] (28%).

So what is common to all these observations is that everyone has acknowledged that there is a significant association between these endocrinal disorders. Studies have also recorded a lower prevalence of thyroid dysfunction in type 2 diabetes mellitus compared to type 1 diabetes mellitus.

The largest community-based study of thyroid dysfunction was carried out in the United States as part of the National Health and Nutrition Examination Survey[46](NHANES III) in 1988 to 1994. The present study compares with NHANES in finding subclinical as the most common disorder. Also, thyroid dysfunctions were more common among women than among men.

In the present study, the type of thyroid dysfunction most common was subclinical hypothyroidism (8%). The general consensus among other studies is that subclinical hypothyroidism is the most common thyroid dysfunction prevalent in type 2 DM. Some studies did not differentiate hypothyroidism further into clinical and subclinical hypothyroidism but none the less stated that hypothyroidism in the most prevalent form of thyroid dysfunction. The percentages reported range from 4.1% by Radaideh AR et al[38] to 17 % by Ramaswamy et al[41] with the exception of the Nigerian study by Udiong CEJ et al[59] (26%) which had included type 1 DM patients as well.

In the subclinical hypothyroidism group, 66 %(16/24) of the patients were females as compared to 33 %(8/24) of males. The total number of females affected was also higher at 67.5% (25/37). This correlates with the study by Nobre EL et al[37] that also stated that females are affected more than males. Akbar DH et al[61] also reported a male to female ratio of 1:1.6. Kiran Babu et al[5] also reported a male to female ratio of 1:2 for hypothyroidism.

After subclinical hypothyroidism the next most prevalent disorder was clinical hypothyroidism in 2.33 %, subclinical hyperthyroidism in 1.33% and clinical hyperthyroidism in 0.67 % of the patients. This was comparable with the study by Perros P[62] in which subclinical hypothyroidism was also followed by clinical hypothyroidism (0.9%), sub clinical hyperthyroidism in 0.5% and clinical hyperthyroidism in 0.5%. The prevalence of hyperthyroidism as reported by Nobre et al[37] was 2 % which was the same as found in the present study.

The Fremantle Diabetes study[63], whose study population includ-

ed only women with type 2 Diabetes Mellitus and which studied only subclinical hypothyroidism, reported a prevalence of 8.6% of subclinical hypothyroidism. Comparing to the present study while the prevalence of subclinical hypothyroidism was 8 % in study population although the prevalence of subclinical hypothyroidism in women was 5.33 %.

The finding increases in significance with the fact that subclinical hypothyroidism has also been named as a risk factor for nephropathy and cardiovascular diseases in type 2 diabetic patients by a study by Jap TS et al.[49]

64 % of the patients with thyroid dysfunction had subclinical hypothyroidism. Although the percentage of reported cases varies the main disorder reported is the same. The present study findings are comparable with Nobre et al [37](68.7%) and Aksar RA et al[65]. This was followed by clinical hypothyroidism. The percentage of cases with clinical hyperthyroidism was still less and clinical hypothyroidism being the least common type of thyroid dysfunction.

Thus it is evident that the studies concurred on the report that hypothyroidism is the thyroid dysfunction most commonly seen in type 2 Diabetes Mellitus and in that sub clinical disorder was the main type of thyroid dysfunction. According to many authors the distinction between clinical and subclinical hypothyroidism might be unjustified as most subclinical patients would progress to overt cases at the rate of 5% per annum. [65] Hence, the need for a means of definitely diagnosing the not so overt or "subclinical" cases, which in many cases will progress to become overt clinical cases in the long run, and hence the need for diagnosing them as soon as possible and instituting proper therapy. Subclinical hyperthyroidism is a heterogeneous clinical entity, and indicates underlying thyroid autonomy (multinodular goiter or a thyroid hormone-producing adenoma), exogenous thyroid hormone administration, early Grave's disease or thyroiditis, and may have important effects on the heart and bony skeleton. However, they occur less frequently than hypothyroid and subclinical cases.[4] However, till date no definite consensus has been reached in the international community with regards to whether or not to treat the subclinical hyperthyroid patients. Most agree that they should be systematically followed up in the future.

Age wise distribution of abnormal thyroid profile

In the present study there were more number of patients with deranged thyroid profile in the age group of 61-70 years and 51 to 60 years (35 % in each category) as compared to the age group of 41 to 50 years (21%). Nobre EL et al[37] also reported that thyroid disease was more in older patients. It may be related to the older age of the type 2 Diabetes Mellitus patients as elderly people are having an increased risk of thyroid disease.[66]

However, no clustering of cases was observed was observed vis a vis subclinical hypothyroidism with regards to a specific age group. It was present in all age groups although the mean age was highest for this group at 61.08 years with a SD of 7.91 years. Similarly the mean age for patients with clinical hypothyroidism was 56 years with a SD of 7.30 years. The mean age for patients with subclinical hypothyroidism was 54.75 years with a SD of 6.65 years. The higher mean age for hypothyroidism as compared to hyperthyroidism also correlates to the study by Arthur MM et al[60] who reported a higher prevalence in elderly women(21%) as compared to younger women(5%).

Distribution of thyroid profile as per BMI

The mean BMI of the euthyroid population was 27.69 with a SD of 12.66. Because of the relationship between obesity, insulin resistance and Type 2 Diabetes Mellitus only 27 % of the patients with deranged thyroid profile had a BMI in the normal range. 32 % of the patients were overweight and another 32 % were obese. 9 % of the patients had morbid obesity. The distribution of patients of any one thyroid dysfunction was not significant with regards to BMI.

Duration of diabetes in patients with thyroid dysfunction

A total of 87.66 % of the patients were euthyroid irrespective of the duration of diabetes. Out of the patients with thyroid dysfunction 27.02 % of the patients were on treatment since less than 5 years. 27.02 % of the patients were on treatment since 5 – 10 years. 35 % of the patients were having a duration of 10 – 15 years and 10.8 % of the patients had duration of diabetes for more than 15 years.

Nobre EL et al[37] did not find a significant difference in the difference in the duration of diabetes and the distribution of thyroid dysfunction. The present study also did not find a significant association between duration of diabetes and thyroid dysfunction.

Mean parameters of different classes

There was no statistically significant difference in the glycemic control of the patients with different types of thyroid dysfunction. The p value for fasting sugar levels is 0.89 with significant being >0.05. The p value for post prandial sugar levels being 0.81 with significant being >0.05. This is as per the findings of Nobre EL et al[37] who did not find significant association with the HbA1c levels and thyroid dysfunction. There was a significant difference in the p values for different classes with regards to the TSH and Free T 4 levels.

Conclusions from different studies

Nobre EL et al[37]:There are few studies on DM2 and thyroid dysfunction; they seem to indicate a higher (12.7%)occurrence of thyroid dysfunction among diabetics when compared with the general population. Our study led to the same conclusion (12.33% of diabetics had thyroid dysfunction). Subclinical Hypothyroidism was the most common type of dysfunction in both studies. The study by Nobre et al[37] did not find any relationship between metabolic control and thyroid function. The high percentage of patients whose thyroid dysfunction was diagnosed 'de novo' may justify routine thyroid function assessments of DM2.

Radaideh AR et al[69]: In T2DM patients, the association of thyroid disease is unexplained. It may be related to the older age of the type T2 DM patients; as elderly people are having an increased risk of thyroid disease.[66,67] The benefits of identifying thyroid dysfunction at an early stage, and even in a symptomatic patient are considerable because progression to overt thyroid dysfunction is associated with consequent morbidity including the adverse effects on lipid[68] and bone metabolism. [69] The study demonstrated a high prevalence of thyroid disease in diabetic patients in comparison with the control group. Screening for thyroid disease in diabetic patients may be justified for early detection and treatment of thyroid dysfunction in diabetic patients in whom thyroid symptoms, if present, may be masked by diabetic state.

Akbar DH et al[61]: The study concluded that thyroid dysfunction and autoimmunity are common in Saudi type 2 diabetics. Further studies are needed on the cost effectiveness of thyroid screening in diabetics.

Perros P et al[62]: The commonest diagnosis was subclinical hypothyroidism (4.8%), followed by hypothyroidism (0.9%), hyperthyroidism 0.5%), and subclinical hyperthyroidism (0.5%). Female patients with Type 1 diabetes had the highest annual risk of developing thyroid disease (12.3%), but all patient groups had a higher incidence of thyroid dysfunction, compared to that reported in the general population. This study suggests that thyroid function should be screened annually in diabetic patients to detect asymptomatic thyroid dysfunction which is increased in frequency in a diabetic population.

Chubb SA et al[63]: Subclinical hypothyroidism was associated with anti-TPO status and age, but there were no independent associations with serum cholesterol, history of coronary heart disease, HbA1c or hypo glycemic therapy. In women with type 2 diabetes without known thyroid disease, subclinical hypothyroidism is a common but incidental finding. As per the study the routine screening of thyroid function in type 2 diabetes is questionable.

Kiran Babu et al[5]: Thyroid dysfunction is common even in type 2 diabetes and is probably unrelated to the autoimmune process. The sex preponderance showed female dominance and thus its cost effective to test for thyroid dysfunction in NIDDM patients.

Arthur MM et al[60]: The study findings support the need for further investigation of the association between diabetes and hypothyroidism in American Indian populations. Hypothyroidism and diabetes share clinical signs and symptoms, such as fatigue, lethargy and weight gain. Populations with diabetes experience very high rates of morbidity and mortality from a variety of disease conditions. The ability to diagnose and treat unsuspected hypothyroidism in these populations may greatly enhance quality of life.

Udiong CEJ et al[59]: The study showed high incidence of abnormal thyroid hormone levels. It recommends routine assessment of thyroid hormone levels in diabetics.

Patricia Wu[70]: In type 2 DM TSH assays should be done at diagnosis and repeated every five years.

CONCLUSIONS :

Among the few studies done on type 2 DM and thyroid dysfunction; they seem to indicate a higher occurrence of thyroid dysfunction among type 2 diabetics. Our work too has led us to the same conclusion (12.33% of diabetics had thyroid dysfunction).

Thyroid dysfunction was seen more in female type 2 DM patients as compared to males.

Subclinical hypothyroidism was the most common type of dysfunction in both males and females.

Thyroid dysfunction was not significantly correlated with duration of diabetes, blood sugar levels and BMI of the patients.

The high percentage of patients whose thyroid dysfunction was diagnosed may justify routine thyroid function assessments of type 2 diabetics.

Further studies are needed on the cost effectiveness of screening for thyroid dysfunction in type 2 DM patients and its benefits.

Graph 1: Age and Sex distribution of studypopulation

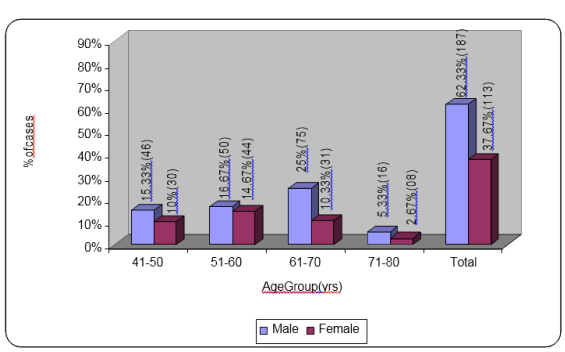

Image1

χ^2-value = 6.84 p-value =0.07 Not Significant,p>0.05

There were total of 300 patients in the study. There were 62.33% males in the studywith a mean age of 56.56 years and a SD of 9.04 years. There were 37.67% females in the study with a mean age of 57.91 years and SD of 7.96years.

Graph 2: : Percentage of cases with deranged thyroidprofile

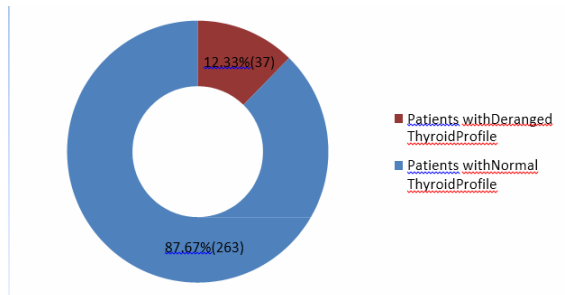

Image2

In all 37 patients out of 300(12.33%) had a deranged thyroid profile. The Zvalue using the Z test for proportion was6.48*.

*z value of more than 1.96 issignificant

Graph 3: Distribution of patients in thestudy

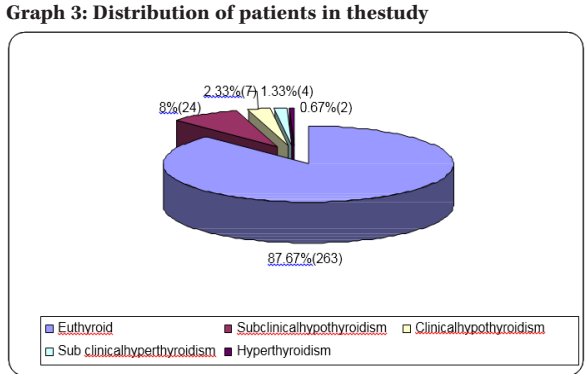

Image3

The most common thyroid dysfunction was subclinical hypothyroidism at 8%(24/300). 7 patients (2.33 %) had clinical hypothyroidism. 4 patientshad subclinical hyperthyroidism while 2 patients had clinicalhyperthyroidism.

Graph 4: Distribution of thyroiddysfunction

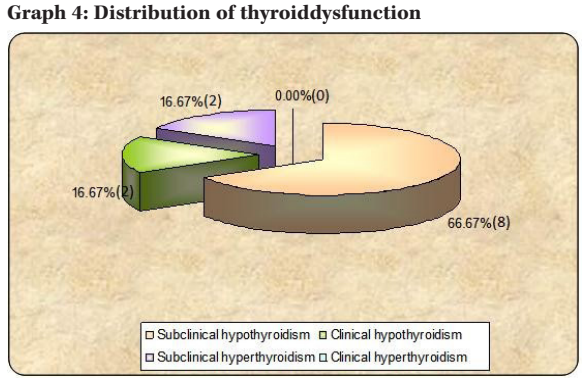

Image4

The most common thyroid dysfunction was subclinical hypothyroidism (64%) followed by clinical hypothyroidism (18.92%). Subclinical hyperthyroidism constituted 10.81% of the cases and

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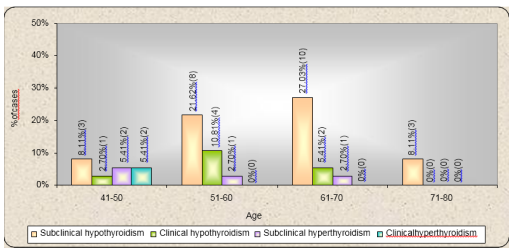
Graph 5A : Age wise distribution of patients with abnormal thyroidprofile



x 2-va lue=12.90, p-value=0.16, Not Significant,p>0.05 The study population was distributed over age group from 40 to 80 years. The mean age of the Sub clinical hypothyroidism group was highest at 61.08 years with a SD of 7.91 years. This was followed by clinical hypothyroidism with a mean age of 56 years and a SD of 7.30 years. The mean age for the subclinical hypo

Graph 5 B : Mean Age of the patients with thyroiddysfunction

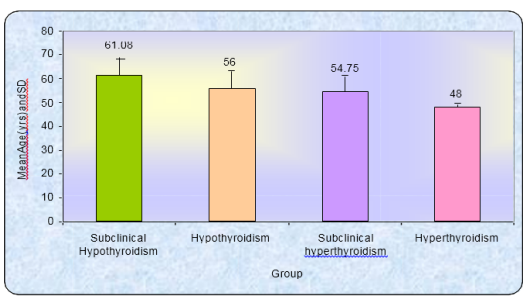


Image5B

Graph 6 : Abnormal Thyroid Dysfunction in MalePopulation

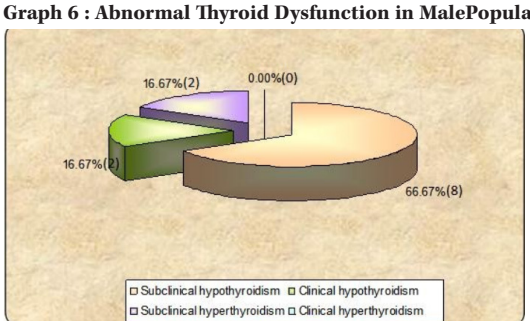


Image6

Subclinical hypothyroidism was the most common disorder in male patients at 66.67%. this was followed by equal percentage of cases(16.67 %) with clinical hypothyroidism and sub clinical hyperthyroidism. Clinical hyperthyroidismwas not detected in male patients in thestudy.

Graph 7 : Abnormal Thyroid Dysfunction in FemalePopulation

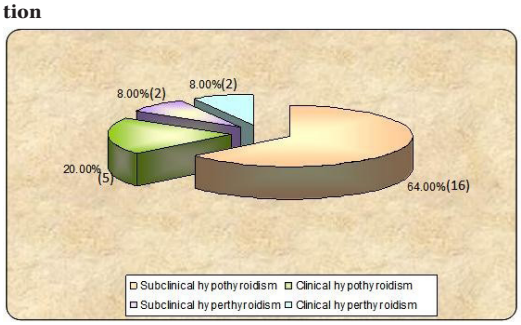


Image7

In the female patients with deranged thyroid profile, 64 % of the patients had subclinical hypothyroidism followed by clinical hypothyroidism in 20 %. Anequal percentage of patients had subclinical hyperthyroidism and clinical hyperthyroidism(8%)

Table 8: Duration of Diabetes in Patients with ThyroidDysfunction

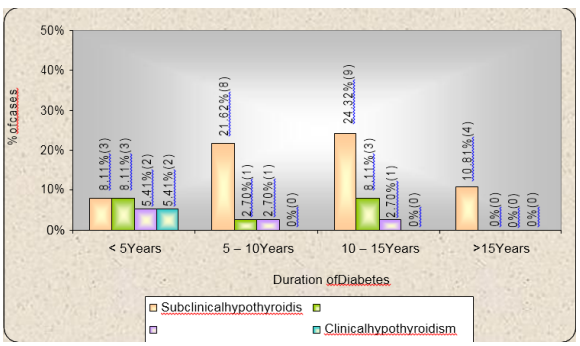


Image8

x2-value=11.71, p = 0.23, Not Significant,p>0.05 The patients with deranged thyroid profile were plotted against the duration of diabetes, with regards to less than 5 years, 5 – 10 years, 10 – 15 years and more than 15 years. The distributionof cases as per increasing duration of diabetes was statistically notsignificant.

Graph 9A: Distribution of thyroid dysfunction as perBMI

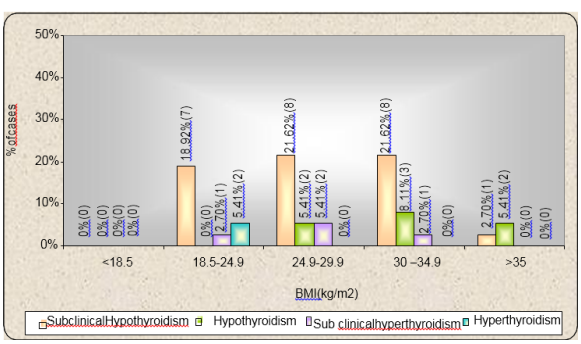


Image9A

x2-value =7.50,p-value=0.27, Not Significant,p>0.05 Mean BMI was highest in patients with hypothyroidism (33.51) with a SD of 5.25. the mean BMI in patients with subclinical hypothyroidism was 28.31 with a SDof

4.95. The mean BMI of patients with clinical hypothyroidism was 28.31 with a SD of 4.95. The mean BMI of patients with sub clinical hypothyroidism andclinical

hypothyroidism was 27.00 and 23.11respectively.

Graph 9 B: Mean BMI of patients with thyroiddysfunction

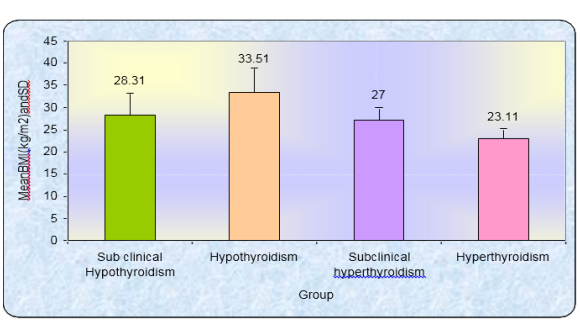


Image9B

Table 10: Mean parameters of differentclasses

	Euthyroid	Subclinical hypo thyroidism	Clinicalhypo Thyroidism	Subclinical hyper thyroidism	Clinicalhyper thyroidism	p-value
Sample size	263	24	7	4	2	-
BSLF	126.71	126.41	131.42	130.25	145.00	0.89 NS,p>0.05
BSL PP	175.79	180.12	179.57	187.25	163.50	0.81 NS,p>0.05
TSH	1.29	7.79	8.04	0.20	0.09	0.00 S,p<0.05
FT4	1.28	1.19	0.24	1.43	3.81	0.00 S,<0.05

Graph 10: Mean parameters of differentclasses

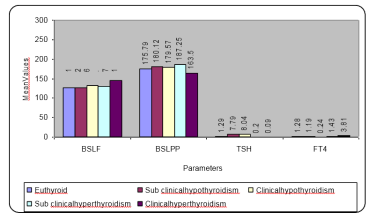


Image10

There was no statistically significant difference in the mean plasma sugar values, bothfasting as well as post prandial in the patients with different type of thyroid dysfunction. However, there was statistically significant difference in the mean TSH and Free T 4 values of the patients.

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