

Thyroid dysfunction in relation to treatment modality in type II diabetes mellitus patients

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Abstract: Hypothyroidism and diabetes share clinical sign and symptoms, such as fatigue, lethargy and weight gain. Thyroid hormones and insulin exert their metabolic effects which are similar in some respects but antagonistic in others, Insulin inhibits glycogenolysis, glycolysis as well as gluconeogenesis. Whereas thyroid hormones has a stimulating effects on this action.

Aims and Objectives: To study the effect of oral hypoglycaemic agents (OHA) and Insulin on thyroid profile of type II diabetes mellitus patients.

Methods: It was a cross sectional study done on type 2 diabetes mellitus patients. 100 cases and 50 controls were included in the study. Diabetic patients on medication that alter thyroid functioning, patients with previously known thyroid dysfunction & pregnant women were excluded from the study. Detailed history was taken; physical examination and required investigations were conducted on patients who satisfied inclusion & exclusion criteria. Investigations done were fasting Plasma glucose, TSH, FT₃ and FT₄. Differences between various parameters were considered statistically significant when the p value was <0.05.

Results: Prevalence of abnormal thyroid function test results was higher in the insulin-treated patients than in those receiving only oral hypoglycaemic agents (OHA) (30.64% vs. 21.05%).

Conclusions: the prevalence of thyroid dysfunction was found to be more in the patients who were on both oral hypoglycaemic agents and insulin than the patients who were only on oral hypoglycaemic agents The present study shows that the prevalence of thyroid dysfunction is high in type 2 DM patients on treatment with insulin, hence regular monitoring of TSH levels in such patients should be suggested.

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I. Introduction

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia, caused either by absolute or relative deficiency of insulin. Lack of insulin affects the metabolism of carbohydrate, protein and fat⁽¹⁾.

It is worth to compare the metabolic effects of insulin with those of thyroid hormones, which may be summarised as follows:-

	Effects of insulin	Effects of thyroid hormones
Carbohydrate metabolism	--	↑
I. Glucose absorption from gut	↑	--
II. Glycogenesis	↓	↑
III. Glycogenolysis	↓	↑
IV. Gluconeogenesis	↓	↑
V. Glycolysis	↓	↑
Lipid metabolism	↑	↓
Lipogenesis	↑	↓
Protein metabolism	↑	↑
Protein synthesis	↑	↑

Thus it is evident that both thyroid hormones and insulin exert their metabolic effects which are similar in some respects but antagonistic in others, Insulin inhibits glycogenolysis, glycolysis as well as gluconeogenesis. Whereas, thyroid hormones have a stimulating effects on these action.

Thus insulin tends to conserve glucose in liver and peripheral tissues thereby keeping the blood glucose level towards the lower side, whereas thyroid hormones tend to increase blood glucose level.⁽²⁾

II. Material And Methods

This Cross-sectional comparative study was carried out on patients of Department of physiology at Rajendra institute of medical science, Ranchi, Jharkhand from November 2013 to January 2015. A total 150 adult subjects (both male and females) of aged ≥ 18 , years were for in this study.

Study Design: Cross-sectional observational study

Study Location: This was a tertiary care teaching hospital based study done in Department of Physiology, at Rajendra institute of medical sciences, Ranchi, Jharkhand.

Study Duration: November 2013 to January 2015.

Sample size: 150 patients.

III. Subjects & selection method:

Selection of cases: Subjects for the study were selected from the Diabetes mellitus patients in the inpatients of medicine and surgery department of Rajendra Institute of Medical Sciences, Ranchi. A total of 100 type 2 diabetic patients who satisfied inclusion and exclusion criteria were included in the study after a well informed consent obtained from them.

Selection of Control :- A total of 50 control were selected of same age group of cases from the attendant of the indoor patients, hospital staff of Rajendra Institute of Medical Sciences, Ranchi. All these individuals were healthy and clinically euthyroid at the time of assessment and there was no history suggestive of thyroid disease. None of these individuals had family history of diabetes mellitus neither of them were taking any drugs including oral contraceptives and had given the consent for the study.

Inclusion criteria:

1. Subjects were diagnosed patients of Type II Diabetes Mellitus who previously had fasting plasma glucose levels of ≥ 126 mg/dl and were receiving treatment such as combination of Insulin and oral hypoglycaemic agents or only oral hypoglycaemic agents.
2. Diabetics irrespective of glucose control.
3. Diabetics Irrespective of their age and sex.
4. Patients had neither sign nor symptoms of thyroid abnormalities or were not assessed earlier.

Exclusion criteria:

1. Pregnant women.
2. Patients on medication that alter thyroid function other than hypoglycaemic drugs and insulin.
3. Diabetic Patients with previously known Thyroid dysfunction

Procedure methodology

The estimation of fasting plasma glucose level was done by GOD/POD method. The serum TSH, FT₃, and FT₄ levels were done by ELISA Microwells method and the readings were taken at 450 nm in a strip ELISA reader.

Statistical analysis

The results were statistically analysed by using the student's t- test and the probability (p value) was calculated using SPSS software. A p-value of <0.001 was taken as highly significant, a p-value of <0.05 as significant and p-value of >0.05 as non-significant.

IV. Result

Table-01: Thyroid dysfunction in relation to treatment of diabetes

Group	Diabetic subjects (n=100)		Percentage of thyroid dysfunction
	Euthyroid	Thyroid dysfunction	
A (pt on OHA) (n=38)	30	8	21.05 %
B (pt on OHA+INS) (N=62)	43	19	30.64 %

The diabetic subject were divided in two groups according to their mode of treatment which were as follows:

Group -- A -- Patients receiving only oral hypoglycaemic agent (OHA).

Group -- B -- Patients receiving both oral hypoglycaemic agents and insulin injection.

Percentage of the patients on treatment with both oral hypoglycaemic agents and insulin injection (62%) were more than the patients on treatment with oral hypoglycaemic agents (38%).

Table shows that in Group-A, 8 out of 38 patients who were only on oral hypoglycaemic agents had thyroid dysfunction, whereas in Group B, 19 out of 62 patients who were on both oral hypoglycaemic agents (OHA) and Insulin injection had thyroid dysfunction.

Prevalence of abnormal thyroid function test results was higher in the insulin-treated patients than in those receiving only oral hypoglycaemic agents (OHA) (30.64% vs. 21.05%).

Table- 02:Serum thyroid hormone levels in Group A and control group

Parameter	Diabetic subjects Group-A (OHA) (n=38) Mean +/- S.D	Non Diabetic subjects (n=50) Mean +/- S.D	't' value	'p' value
TSH	5.189+/-4.798	2.075+/-1.283	4.394	0.0001
FT ₃	2.222+/-1.236	2.676+/-0.832	2.057	0.0429
FT ₄	1.189+/-0.59	1.463+/-0.344	2.732	0.007

Present study shows that the levels of TSH (5.18+/-4.79) in case group was significantly higher (p<0.0001) than the control group (2.07+/-1.28) while FT₃ (2.22+/-1.23) in case group was significantly lower (p=0.04) than control group (2.67+/-0.83) and FT₄ (1.18+/-0.59) in case group was significantly lower (p=0.007) than control group (1.46+/-0.34).

So, the Thyroid profile of Group-A diabetic subject shows low thyroid hormone level as compared to normal healthy non diabetic control.

Table-03:Serum thyroid hormone levels in Group B and control group

Parameter	Diabetic subjects Group-B (OHA+INS) (n=62) Mean +/- S.D	Non Diabetic subjects (n=50) Mean +/- S.D	't' value	'p' value
TSH	5.413+/-4.783	2.075+/-1.283	4.794	0.0001
FT ₃	2.166+/-1.458	2.676+/-0.832	2.20	0.03
FT ₄	1.148+/-0.592	1.463+/-0.344	3.336	0.0012

Present study shows that the levels of TSH (5.41+/-4.78) in case group was significantly higher (p<0.0001) than the control group (2.07+/-1.28) while FT₃ (2.16+/-1.45) in case group was significantly lower (p=0.03) than control group (2.67+/-0.83) and FT₄ (1.14+/-0.59) in case group was significantly lower (p=0.001) than control group (1.46+/-0.34).

So, the Thyroid profile in Group-B diabetic subject shows low thyroid hormone level as compared to normal healthy non diabetic control.

Table- 04:Serum thyroid hormone levels in both groups

Parameter	Diabetic subjects Group-A (OHA) (n=38) Mean +/- S.D	Diabetic subjects Group-B (OHA+INS) (n=62) Mean +/- S.D	't' value	'p' value
TSH	5.189+/-4.798	5.413+/-4.783	0.227	0.821
FT ₃	2.222+/-1.236	2.166+/-1.458	0.197	0.843
FT ₄	1.189+/-0.59	1.148+/-0.592	0.336	0.736

Present study shows that the levels of TSH, FT₃ and FT₄ in group-A diabetic subject were (5.18+/-4.79), (2.22+/-1.23) and (1.189+/-0.59) respectively while the level of TSH, FT₃ and FT₄ in group-B diabetic subject were (5.41+/-4.78), (2.16+/-1.45) and (1.14+/-0.59) respectively.

The differences between mean TSH, FT₃ and FT₄ of Group-A and Group-B diabetic subject were not significant (P>0.05).

V. Discussion

In the present study 100 cases of Type- II Diabetes Mellitus were selected for the study of thyroid hormone levels. All these patients were confirmed diabetics who previously had fasting plasma glucose levels of ≥ 126 mg/dl and were receiving treatment such as combination of Insulin and oral hypoglycaemic agents or only oral hypoglycaemic agents (OHA). The above diabetics were compared to 50 normal non diabetic control subjects and also the both groups of subject taking oral hypoglycaemic and insulin were compared.

According to Table-01, the diabetic subjects were divided in two groups according to their mode of treatment which were as follows:

Group -- A -- Patients receiving only oral hypoglycaemic agents (OHA).

Group -- B -- Patients receiving both oral hypoglycaemic agents and insulin injection.

In the study out of 27 diabetic patients who had thyroid disorder, 8 (21.05%) were on oral hypoglycaemic agents and 19 (30.64%) were on both oral hypoglycaemic agents and insulin.

Study of thyroid hormone levels in group A (patients on OHA) with controls showed low thyroid hormone levels in group-A diabetic subjects as compared to normal healthy non diabetic controls.

Study of thyroid hormone levels in group B (patients on OHA and insulin) with controls showed low thyroid hormone levels in group-B diabetic subjects as compared to normal healthy non diabetic controls.

On comparison of both the Group A and Group B we observed that the prevalence of thyroid disorder was found to be more in Group B who were on both oral hypoglycaemic agents and insulin but the differences between mean TSH, FT₃ and FT₄ of both groups was not statistically significant as shown in table-04.

Thus present study further suggests that insulin has more deteriorating effect on thyroid functions in comparison to oral hypoglycaemic agents.

This was in accordance with the findings of Celani MF et al⁽³⁾ who found prevalence of thyroid dysfunctions more in patients who were on insulin therapy.

The abnormal thyroid hormone levels may be the outcome of the various medications the diabetics were receiving. For example, it is known that insulin, an anabolic hormone, enhances the levels of FT₄ while it suppresses the levels of T₃ by inhibiting hepatic conversion of T₄ to T₃. On the other hand, some of the oral hypoglycaemic agents such as the phenylthioureas are known to suppress the levels of FT₄ and T₄, while raising the levels of TSH.

The thyroid hormone levels FT₃ and FT₄ in diabetic subjects were significantly lower than the normal healthy non diabetic control group which was in accordance with SandipSendhav et al⁽⁴⁾, Pasupathi et al⁽⁵⁾, C.E.J. Udiong et al⁽⁶⁾ and VinuVij et al⁽⁷⁾ in which they also showed statistically significant low thyroid hormone level in diabetes mellitus patient as compared to normal healthy control.

In many earlier studies done by SandeepSendhavetal⁽⁴⁾, Bharat eta al⁽⁸⁾, Mushir Ahmad et al⁽⁹⁾, total T₃ and T₄ were investigated but in the present study we opted to investigate FT₃ and FT₄ in the subjects as the total thyroid hormone (T₃ & T₄) concentration is dependent on the concentration of thyroid binding proteins. Thus any condition that affects the level of thyroid binding protein will affect the total thyroid hormone level. In opposite to it the free thyroid hormones (FT₃ & FT₄) is not affected by changes in the concentration of thyroid binding protein and so the free thyroid hormones assay generally are considered to provide more reliable indicator of true thyroid status.⁽¹⁰⁾

VI. Conclusion

In this study we conclude that the prevalence of thyroid disorder was found to be more in the patients who were on both insulin and oral hypoglycaemic agents (OHA) than the patients who were only on oral hypoglycaemic agents alone though the difference was not statistically significant. Thus a systemic approach to thyroid testing in diabetic subject is favourable, however no definitive guideline exist regarding screening for thyroid dysfunction in diabetic patients. So it is suggested that regular screening for thyroid abnormalities in all diabetic patients will allow early treatment of thyroid dysfunction in these population and may greatly enhance the quality of life.

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