

## Thyroid Status and Dyslipidemia in Type 2 Diabetic and Non-Diabetic Population

Priti Singh<sup>1\*</sup>, Salman Khan<sup>2</sup>, Rashmi<sup>3</sup>, Rabindra Kumar Mittal<sup>4</sup>

1- Lecturer, Department of Biochemistry, Nepalgunj Medical College, Nepal

2- Assistant professor, Department of Microbiology, Nepalgunj Medical College, Nepal

3- Department of Microbiology, Kasturba Medical College, Mangalore, India

4- Professor, Department of Biochemistry, Nepalgunj Medical College, Nepal

### \*Correspondence:

Priti Singh, Lecturer, Department of Biochemistry, Nepalgunj Medical College, Nepal

Email: priti186631@gmail.com

Tel: (977) 984 835 4981

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### Abstract

**Objective:** Thyroid dysfunction complicates the metabolic derangement observed in Diabetes Mellitus (DM). It is necessary to recognize and treat it, when present, in order to achieve stability of metabolic control in these patients. The aim of this study was to investigate the effect of DM on thyroid hormone levels and other biochemical variables.

**Materials and Methods:** To determine the incidence of abnormal thyroid hormone levels in diabetics in Nepalgunj medical college and Hospital (Nepal), blood samples from 100 diabetic subjects and 100 non-diabetic controls were taken between 1st February, 2012 to 31st January, 2013 for investigation of free triiodothyronine (FT3), free thyroxine (FT4), thyroid stimulating hormone (TSH), fasting plasma glucose (FPG), serum cholesterol, serum triglycerides, high density lipoprotein (HDL), low density lipoprotein (LDL), very low density lipoprotein (VLDL), blood urea, serum creatinine, total protein, albumin, serum glutamate oxaloacetate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT).

**Results:** Our findings showed that the level of FT3 and FT4 were significantly lower while the level of TSH was significantly higher in type 2 diabetics as compared to non-diabetics. From the 100 diabetic subjects that were studied, 29% showed abnormal thyroid hormone levels (24% hypothyroidism and 5% hyperthyroidism). The incidence of hypothyroidism was more in females (16%) as compared to males (8%) in type 2 diabetes.

**Conclusion:** Failure to recognize the presence of these abnormal thyroid hormone levels in diabetics may be a primary cause of poor management often encountered in some treated diabetics.

**Keywords:** Diabetes mellitus type 2, Dyslipidemia, Thyroid hormones.

### Introduction

Diabetes mellitus is an important health problem affecting major populations worldwide. It is characterized by absolute or relative deficiencies in insulin

secretion and/or insulin action associated with chronic hyperglycemia and disturbances of carbohydrate, lipid, and protein metabolism. Defects in carbohydrate metabolizing

machinery and consistent efforts of the physiological system to correct the imbalance in carbohydrate metabolism place an overexertion on the endocrine system. Continuing deterioration of endocrine control exacerbates the metabolic disturbances and leads primarily to hyperglycemia (1-3). The physiological and biochemical interrelationship between insulin and iodo-thyronines, and the influence of both them on the metabolism of carbohydrates, proteins, and lipids has been recorded (4). Thyroid disorders are very common in the general population and it is only at the second place to diabetes as the most common condition affecting the endocrine system. As a result, it is common for an individual to be affected by both thyroid diseases and diabetes. The first report showing the association between diabetes and thyroid dysfunction was published in 1979 (5-6). Since then, a number of studies have estimated the prevalence of thyroid dysfunction among diabetic patients to be varying from 2.2% to 17% (7-8). However, fewer studies have estimated much higher prevalence of thyroid dysfunction in diabetes (i.e. 31% and 46.5% respectively)(9-10). To the best of our knowledge, no studies have been done to compare the thyroid dysfunction in diabetic and non-diabetic subjects in mid- and far-western regions of Nepal. Therefore, the aim of the present study was the comparison of thyroid hormone levels and other biochemical variables in diabetic and non-diabetic population attending an outpatient department.

### Materials and Methods

It was a case-control study. The study population consisted of 200 subjects (age- and sex-matched) including two groups: diabetic (n=100) and non-diabetic (n=100).

Confirmed diabetic cases on oral hypoglycemic agent and having Fasting Plasma Glucose more than 110 mg/dl were included in this study. Those patients were using insulin, having diseases that may affect thyroid function and on medications that can

affect thyroid function excluded from this study.

This study was carried out in the central laboratory of biochemistry of Nepalgunj Medical College and Hospital between 1st February, 2012 and 31st January, 2013. Randomly blood samples from subjects and controls were taken for investigation of free tri-iodothyronine (FT3), free thyroxine (FT4), thyroid stimulating hormone (TSH), fasting plasma glucose (FPG) and post prandial glucose, serum cholesterol, serum triglycerides, high-density lipoprotein(HDL), low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), blood urea, serum creatinine, total protein, albumin, serum glutamate oxaloacetate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT). The estimation of serum FT3, FT4 and TSH were made by the enzyme immunoassay method, using Randox kits (Randox Laboratories Ltd, Ardmore, UK). Blood glucose, cholesterol, triglycerides, HDL, LDL, VLDL, blood urea, serum creatinine, total protein, albumin, SGOT and SGPT were determined using a fully automated clinical chemistry analyzer. Ethical approval for the study was taken from the institutional research ethical committee. The normal level of serum FT3 was 1.5-4.2 pg/ml, FT4 was 0.8-1.68 ng/dl and TSH was 0.2-5.2 mIU/L.

The following guidelines for detection of thyroid dysfunction were considered: 1) Normal-when FT3, FT4, and TSH were within the normal range; 2) Primary hypothyroidism-when TSH was more than 5.2 mIU/L, and FT3 and FT4 were less than the normal values; 3) Primary hyperthyroidism-when TSH was less than 0.2 mIU/L, and FT3 and FT4 were more than the normal values; 4) Subclinical hypothyroidism-when TSH was more than 5.2 mIU/L, and FT3, FT4, T3 and T4 were within the normal range; and 5) Subclinical hyperthyroidism-when TSH was less than 0.2 mIU/L and FT3 and FT4 were within the normal range.

The results obtained from the above investigation were analyzed and expressed as mean  $\pm$  SD and student t-test was used for comparison of some parameters by using the Statistical Package for Social Sciences (SPSS) software (version 16, SPSS, Inc., Chicago, IL, USA).

## Results

Both type 2 diabetic subjects and non-diabetic controls included 50 male and 50 females with mean age of  $48.05 \pm 11.72$  and  $47.76 \pm 11.78$  years, respectively.

FPG, serum cholesterol, triglycerides, VLDL, creatinine, blood urea, SGOT and SGPT were significantly higher in diabetic subjects as compared to non-diabetic controls while serum HDL, total protein and albumin were significantly lower in diabetic patients as compared to non-diabetic controls (Table 1).

The serum levels of FT3 and FT4 were significantly lower in diabetic subjects as compared to non-diabetic subjects while serum TSH level was significantly higher in diabetic subjects in comparison to non-diabetic subjects (Table 2).

Out of 100 type 2 diabetic subjects studied, 29% showed abnormal thyroid functions (24%

had low and 5% high thyroid hormone levels); 71% had normal thyroid hormone level. The incidence of hypothyroidism was seen higher in females (16%) than in males (8%) and hyperthyroidism was also seen more in females (3%) than in males (2%) as shown in Figure 1.

## Discussion

In our study, FPG, postprandial glucose, serum cholesterol, serum triglycerides, serum LDL, serum VLDL, serum creatinine, blood urea, SGOT and SGPT were significantly higher in diabetic subjects as compared to non-diabetic subjects while serum HDL, total protein and albumin were significantly lower in diabetic subjects as compared to non-diabetic subjects. In this study, diabetic subjects showed significantly higher serum levels of cholesterol, triglycerides, LDL and VLDL, as well as lower level of HDL in comparison to non-diabetic subjects. Our results are in consistence with previous cross-sectional study conducted among young adult population by Sawant et al. (11). The abnormally high concentration of serum lipid in diabetes is mainly due to the increase in mobilization of free fatty acids from peripheral

**Table 1. Comparison of biochemical changes in non-diabetic and diabetic subjects**

Parameter	Diabetic subjects	Non-diabetic controls	P-value
Fasting plasma glucose (mg/dl)	161.77 $\pm$ 20.57	90.63 $\pm$ 6.17	<0.0001
Postprandial glucose (mg/dl)	322.48 $\pm$ 35.87	125.52 $\pm$ 21.51	<0.0001
Blood Urea (mg/dl)	35.67 $\pm$ 20.60	27.44 $\pm$ 10.10	$\approx$ 0.0004
Serum creatinine (mg/dl)	1.14 $\pm$ 0.25	0.87 $\pm$ .267	<0.0001
Total cholesterol (mg/dl)	180.67 $\pm$ 13.38	166 $\pm$ 10	<0.0001
Triglyceride (mg/dl)	164.60 $\pm$ 33.34	123.76 $\pm$ 33.34	<0.0001
HDL-C (mg/dl)	39.97 $\pm$ 8.55	42.15 $\pm$ 3.82	$\approx$ 0.0209
LDL-C (mg/dl)	107.78 $\pm$ 24.07	99.10 $\pm$ 20.01	$\approx$ 0.0061
VLDL-C (mg/dl)	35.67 $\pm$ 11.60	26.15 $\pm$ 6.32	<0.0001
Total protein (g/dl)	6.1 $\pm$ 1.63	7.06 $\pm$ 0.59	<0.0001
Albumin (g/dl)	3.35 $\pm$ 0.61	4.33 $\pm$ 0.33	<0.0001
SGOT (U/L)	35.43 $\pm$ 6.82	31.68 $\pm$ 4.8	<0.0001
SGPT (U/L)	39.24 $\pm$ 7.32	33.63 $\pm$ 4.46	<0.0001

HDL-C=High-density lipoprotein-cholesterol; LDL-C=Low-density lipoprotein-cholesterol; VLDL-C=Very low-density lipoprotein-cholesterol; SGOT= Serum glutamate oxaloacetate transaminase; SGPT= Serum glutamate pyruvate transaminase

**Table 2. Serum thyroid hormone levels in non-diabetic and diabetic subjects**

Thyroid Hormones	Diabetic subjects	Non-diabetic controls	P-value
FT3 (pg/ml)	2.57 $\pm$ 0.74	3.01 $\pm$ 0.99	<0.0001
FT4 (ng/dl)	1.32 $\pm$ 0.27	1.43 $\pm$ 0.46	0.0405
TSH (U/ml)	5.54 $\pm$ 2.24	2.89 $\pm$ 1.31	<0.0001

FT3= Free tri-iodothyronine; FT4= Free thyroxine; TSH=Thyroid stimulating hormone

fat depots (12). Insulin resistance, an important factor in type 2 diabetes mellitus, leads to excessive liberation of free fatty acids from adipose tissue (13,14), which activates the signaling enzyme protein kinase C, that in turn inhibits phosphatidylinositol-3 (PI-3) kinase (an eNOS agonist pathway) and thus increase the production of reactive oxygen species. This mechanism directly impairs nitric oxide (NO) production or decreases its bioavailability once produced (15).

There was also significant increase in blood urea and serum creatinine in diabetic patients compared to non-diabetic controls. The above results corresponded with the finding of Mittal et al. (16) in which the mean values for serum creatinine ( $1.14 \pm 0.25$  mg/dl) were increased in diabetic subject as compared to non-diabetic controls ( $0.87 \pm 0.267$  mg/dl).

There was also significant increase in SGOT and SGPT in type 2 diabetic patients as compared to non-diabetic controls. These results are in accordance with the findings of Idris et al. (17) who found that the levels of SGOT and SGPT in type 2 Sudanese diabetic patients were significantly higher as compared to non-diabetic controls.

The serum levels of FT3 and FT4 were significantly lower in diabetic subjects as compared to non-diabetic subjects while level of serum TSH was significantly higher in

diabetic subjects as compare to non-diabetic subjects. The bulk of the hormones secreted by follicular cells of the thyroid gland are released in the free form into plasma where it becomes largely bound to thyroid binding globulin (TBG) and to some extent to pre-albumin and albumin. A small fraction circulates free in plasma (FT4). Suzuki et al. (18) attributed the abnormal thyroid hormone levels found in diabetes to the presence of Thyroid Hormone Binding Inhibitor (THBI), an inhibitor of extrathyroidal conversion enzyme of T4 to T3, and dysfunction of the hypothalamus-hypophyseal-thyroid axis. These situations may prevail in diabetics and would be aggravated in poorly controlled diabetics. Stress, which is associated with diabetes mellitus, may also cause changes in the hypothalamus-anterior pituitary axis in these diabetics. It appears that the presence of subclinical hypothyroidism and hyperthyroidism may result from hypothalamus-hypophyseal-thyroid axis disorders as suggested by Celani et al. (19). Suggestion was made that the finding of definite hypothyroidism or hyperthyroidism be given adequate attention and treatment of the thyroid disorder appropriately undertaken (20).

## Conclusion

This study showed a high incidence of

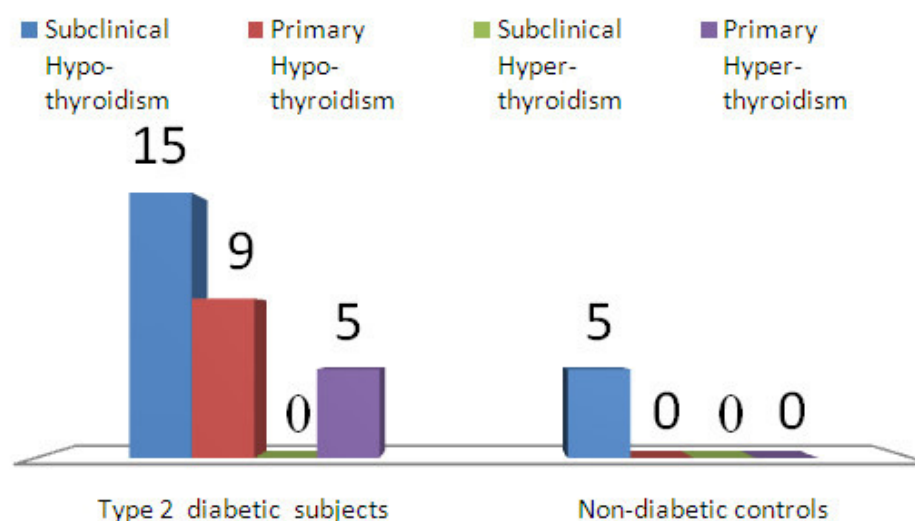


Figure 1. Thyroid status in type 2 diabetic and non-diabetics subjects

abnormal thyroid hormone levels among diabetic patients as compared to non-diabetics. In conclusion, our findings demonstrate that detection of abnormal thyroid hormone levels in addition to other biochemical variables in the early stage of diabetes will help patients improve their health and reduce their morbidity rate.

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