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Evolution of thyroid dysfunction among type-2 diabetic mid and far western Nepalese population

Priti Singh[1*], Salman Khan[2], Rabindra Kumar Mittal[1]

[1]*Department of Biochemistry, Nepalgunj Medical College, Affiliated to Kathmandu University, Nepal*

[2]*Department of Microbiology, Nepalgunj Medical College, Affiliated to Kathmandu University, Nepal*

PEER REVIEW

Peer reviewer

Dr. M. Amuba Singh, Professor and Head of Biochemistry, Regional Institute of Medical Sciences, Imphal, Manipur, India.
Tel: +91 943 603 7345
Fax: +91 385 241 4625
E-mail: amubam@gmail.com

Comments

The work is a good study whereby the authors could find out an association of abnormal thyroid disorders in T2D. The result reveals a higher incidence in the Western Nepal. It is significant to mention that the inhabitants of the area mainly consume a good amount of leafy vegetables which may reflect their thyroid status. Further studies are needed in large population to account for the relationship and association of the thyroid disorders and T2D.
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ABSTRACT

Objective: To evaluate the prevalence of thyroid dysfunction in subjects with type 2 diabetes and the effect of type 2 diabetes mellitus (T2D) on other biochemical variables.

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 (FT_3), free thyroxine (FT_4), thyroid stimulating hormone (TSH), plasma glucose fasting, serum cholesterol, serum triglycerides, high density lipoprotein, low density lipoprotein, very low density lipoprotein, blood urea, serum creatinine, total protein and albumin. Randox kits obtained from Randox Laboratories Ltd., Ardmore, UK were used for the analysis of FT_3, FT_4 and TSH.

Results: Our findings showed that the level of FT_3 and FT_4 were significantly lower while the level of TSH was significantly higher in T2D as compared to non-diabetics. From the 100 diabetic subjects studied, 29% showed abnormal thyroid hormone levels (24% hypothyroidism and 5% hyperthyroidism).

Conclusions: Our findings indicate that the frequency of thyroid is significantly higher in type 2 diabetic patients than in non-diabetic control group. Further studies are required to recognize the cause of hypothyroidism in T2D.

KEYWORDS

Type 2 diabetes mellitus, Thyroid hormones, Hypothyroidism

1. Introduction

Thyroid dysfunction is a spectrum of disorders of the thyroid gland which manifests either as hyper or hypothyroidism and is reflected in the circulating levels of thyroid stimulating hormone (TSH)[1]. Thyroid hormones, namely Triiodothyronine (T3) and Thyroxine (T4); either or both of which may be elevated or reduced have both direct and indirect effects on blood glucose homeostasis[2]. Elevated levels of free circulating thyroid hormones (hyperthyroidism) produce hyperglycaemia by causing polyphagia, enhancing glucose absorption from the gastro-intestinal tract, accelerating insulin degradation and stimulating glycogenolysis[3]. Reduced levels of the hormones (hypothyroidism) may cause hypoglycaemia[4]. Diabetic patients have a higher prevalence of thyroid disorders compared with the general population because patients with one organ-specific autoimmune disease are at risk of developing other autoimmune disorders[5,6]. A number of reports have also indicated a higher than normal

*Corresponding author: Ms. Priti Singh, Lecturer, Department of Biochemistry, Nepalgunj Medical College, Chisapani, Banke, Nepal.
Tel: 009779848354981
E-mail: priti186631@gmail.com
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prevalence of thyroid disorders in type 2 diabetic patients, with hypothyroidism being the most common disorder[7]. The first report showing the association between diabetes and thyroid dysfunction were published in 1979[8,9]. Since then a number of studies have estimated the prevalence of thyroid dysfunction among diabetes patients to be varying from 2.2% to 17%[10,11]. However, fewer studies have estimated much higher prevalence of thyroid dysfunction in diabetes *i.e.* 46.5% and 31% respectively[2,12]. In addition, diabetic women are more frequently affected than men and hypothyroidism is more common than thyrotoxicosis. It has been showed that subclinical hypothyroidism affects almost one in 20 women with type 2 diabetes (T2D)[12]. To the best of our knowledge, no studies have been done to estimate the prevalence of thyroid dysfunction in type 2 diabetic patients in mid and far western region of Nepal. Therefore, the aim of the present study was to determine the prevalence of thyroid dysfunction in patients with T2D attending in and outpatient clinic.

2. Materials and methods

The study population consisted of 200 subjects (age-matched and sex-matched) divided into two groups: diabetic subjects (n=100) and non-diabetic controls (n=100). This study was carried out in the Central Laboratory of Biochemistry of the Nepalgunj Medical College and Hospital between 1st February, 2012 to 31st January, 2013. Blood samples from subjects and controls were taken for investigation of free triidothyronine (FT_3), free thyroxine (FT_4), TSH, plasma glucose fasting, serum cholesterol, serum triglycerides, high density lipoprotein (HDL), low density lipoprotein (LDL), very low density lipoprotein (VLDL), blood urea, serum creatinine, total protein and albumin. The estimation of serum free T3, free T4 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 and albumin were determined using a fully automated clinical chemistry analyzer. Ethical approval for the study was taken from the institutional research ethical committee.

The normal levels of serum FT_3 was 1.5-4.2 pg/mL, FT_4 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 FT_3, FT_4, and TSH were within the normal range; 2) Primary hypothyroidism-when TSH is more than 5.2 mIU/L and FT_3, FT_4 are less than the normal value; 3) Primary hyperthyroidism-when TSH is less than 0.2 mIU/L and FT_4, FT_3, are more than the normal values; 4) Subclinical hypothyroidism-when TSH is more than 5.2 mIU/L and FT_3, FT_4, T3, T4 are within the normal range; 5) Subclinical hyperthyroidism-when TSH is less than 0.2 mIU/L and FT_3, FT_4 are within the normal range. The results obtained from the above investigation were analyzed and expressed as mean±SD by using Excel 2007. The comparison was done by student's t-test on number of variable of each parameter using SPSS version 16.

3. Results

The sex and age distribution of non-diabetic and diabetic subjects were recorded. Both type 2 diabetic subjects and non diabetic controls included 50 male and 50 females with mean age of (48.05±11.72) and (47.76±11.78) years respectively.

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

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

Parameter	Non-diabetic controls	Diabetic patients subjects	P-value
Fasting (mg/dL)	90.630±6.170	161.770±20.570	<0.000 1
Urea (mg/dL)	27.440±10.100	35.670±20.600	<0.000 4
Creatnine (mg/dL)	0.870±0.267	1.140±0.250	<0.000 1
Total cholesterol (mg/dL)	166.000±10.000	180.670±13.380	<0.000 1
Triglyceride (mg/dL)	123.760±33.340	164.600±33.340	<0.000 1
HDL-C (mg/dL)	42.150±3.820	39.970±8.550	<0.020 9
LDL-C (mg/dL)	99.100±20.010	107.780±24.070	<0.006 1
VLDL-C (mg/dL)	26.150±6.320	35.670±11.600	<0.000 1
Total protein (g/dL)	7.060±0.590	6.100±1.630	<0.000 1
Albumin (g/dL)	4.330±0.330	3.350±0.610	<0.000 1

The serum levels of free T3, free T4 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 (Table 2).

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

Thyroid hormones	Diabetic subjects	Non-diabetic controls	P-value
Free T3	2.57±0.74	3.01±0.99	<0.000 1
Free T4	1.32±0.27	1.43±0.46	<0.040 5
TSH	5.54±2.24	2.89±1.31	<0.000 1

Out of 100 type 2 diabetic subjects, 29% showed abnormal thyroid functions (24% had low thyroid hormone level and 5% had high thyroid hormone level) and 71% showed normal thyroid hormone level as shown in Figure 1 and Table 3.

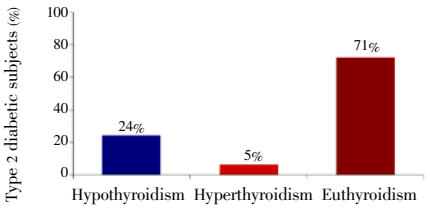

Figure 1. Prevalence of thyroid dysfunction among T2D.

Table 3
Type of thyroid disorders according to gender in type 2 diabetic and non diabetic group.

Distribution of subjects		Types of thyroid disorders			
		Subclinical hypothyroidism	Primary hypothyroidism	Subclinical hyperthyroidism	Primary hyperthyroidism
Type 2 diabetic subjects	Male	5	3	0	2
	Female	10	6	0	3
Non-diabetic controls	Male	2	0	0	0
	Female	3	0	0	0

4. Discussion

In this study, diabetic subjects showed significant higher serum levels of cholesterol, triglycerides, VLDL and lower level of HDL as compared to non diabetic subjects. Our results are in consistence with previous cross sectional study conducted among young adult population by Sawant *et al.*[13], where increase prevalence of dyslipedemia was found to be the major contributor of cardio vascular disorder. The abnormally high concentration of serum lipid in diabetes is mainly due to the increase in mobilization of free fatty acids from peripheral fat depots[14]. Insulin resistance, an important factor in T2D, leads to excessive liberation of free fatty acids from adipose tissue[15,16], which activates the signaling enzyme protein kinase C, inhibits phosphatidylinositol-3 (PI-3) kinase (an eNOS agonist pathway), and increases the production of reactive oxygen species. This mechanism directly impairs nitric oxide production or decreases its bioavailability once produced[17]. There was also significant decrease in level of total protein and albumin in diabetic patients when compared with non-diabetic subjects. These results are in accordance with the findings of Pasupathi *et al.* who found that the levels of total protein and albumin in type 2 South Indian diabetic patients were significantly lower as compared to non diabetic controls[18].

The present study reported high incidence of abnormal thyroid hormone level in type 2 diabetic population. Our observation is in agreement with reports of Suzuki *et al.*, Celani *et al.*, and Udiang *et al.* who in separate studies found altered thyroid hormone level of different magnitude in diabetic patients[2,12,19].

Another study by Papazafiropoulou *et al.* in a randomly selected group of 1 310 diabetic adults estimated that the prevalence of thyroid dysfunction was found to be 13.4%[10]. A recent study reported that thyroid dysfunction was present in 16% of Saudi T2D patients[20]. Also, a study in Jordan showed that the overall prevalence of thyroid dysfunction was 12.5% in T2D patients[21]. In our study, we reported a higher prevalence of thyroid dysfunction among diabetic females. It is well established that hypothyroidism is more common in diabetic females. In a study by Papazafiropoulou *et al.*, the prevalence of thyroid dysfunction was 10.9% in females and 6.9% in males[10]. The NHANES III study reported that the prevalence of subclinical hypothyroidism was 3.4% in males and 5.8% in females[22]. In addition, a study in 420 adult females with T2D randomly selected from participants in the community-based Fremantle diabetes study showed that the prevalence of subclinical hypothyroidism was 8.6%[23]. Finally, a recent study revealed that the prevalence of subclinical hypothyroidism was 5.2% in males and 8.4% in females with T2D[24].

The present study reveals different grades of thyroid dysfunction among diabetes. Hypothyroidism is present in 24% (15% subclinical hypothyroidism and 9% primary hypothyroidism) and hyperthyroidism is present in 6.25% (all primary hyperthyroidism) of diabetic subjects. This goes in accordance with the reports of Suzuki *et al.* and Smithson *et al.*, who in separate studies found altered thyroid hormone level of different magnitude (both low and high) in diabetic patient[11,19] . The high prevalence of abnormal thyroid hormone levels in connection with the local diets of the people of Western Nepal require further research attention as most foods are leafy. These local diets may also influence thyroid hormone levels at the thyroid, hypothalamus or insulin levels.

In conclusion, this study shows high incidence of abnormal thyroid hormone level among type 2 diabetic subjects. Failure to recognize the presence of abnormal thyroid hormone level in type 2 diabetes may be a primary cause of poor management often encountered in some treated T2D. There is therefore a need for the routine assay of thyroid hormones in type 2 diabetic, particularly in those patients whose conditions are difficult to manage.

Conflict of interest statement

We declare that we have no conflict of interest.

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Comments

Background

T2D is common in Western Nepal. The present study aims at finding out a close relationship between diabetes and thyroid abnormalities.

Research frontiers

Although many studies are available to sort association between diabetes and thyroid abnormalities in other parts of the globe, no such attempt has been made in Western Nepal.

Related reports

Many researchers have found out association of thyroid abnormalities in T2D to an extent of 16%. Whereas the present study could find out a higher incidence of 24% as hypothyroidism. The difference may be due to the dietary habits of the diabetics in Western Nepal.

Innovations & breakthroughs

Association of thyroid abnormalities may be suspected in type 2 diabetic subjects. This will help the patients from developing thyroid abnormalities thereby preventing themselves from complications.

Applications

The study results would definitely help the diabetic patients to modify their dietary habits to prevent themselves from developing abnormal thyroid function.

Peer review

The work is a good study whereby the authors could find out an association of abnormal thyroid disorders in T2D. The result reveals a higher incidence in the Western Nepal. It is significant to mention that the inhabitants of the area mainly consume a good amount of leafy vegetables which may reflect their thyroid status. Further studies are needed in large population to account for the relationship and association of the thyroid disorders and T2D.

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