

# Spectrum of Thyroid Disorders in Patients with Type-2 Diabetes Mellitus

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## ABSTRACT

**Background:** Diabetes mellitus and thyroid disorders are the two most common endocrine disorders and they mutually affect each other. There are very few researches from Nepal that have evaluated the association of type-2 diabetes mellitus and thyroid dysfunction. The main objective of this study was to evaluate the prevalence and spectrum of thyroid dysfunctions among type-2 diabetes mellitus patients.

**Methods:** This was cross-sectional study conducted among 204 type-2 diabetes mellitus patients visiting the internal medicine department of a tertiary center located in Kathmandu, Nepal.

**Results:** The prevalence of thyroid disorders in patients with type-2 diabetes mellitus was 27.94%. Subclinical hypothyroidism, which occurred in 14.71% of patients, was the most common thyroid disorder. The longer duration of diabetes, more than ten years, was associated with the increased thyroid disorders ( $p=0.025$ ). The poor glycemic control,  $HbA1c \geq 7\%$ , was associated with significantly increased prevalence of thyroid dysfunction in type-2 diabetes mellitus patients ( $p=0.002$ ). Female patients had higher prevalence of thyroid disorders than males, but this association was not statistically significant.

**Conclusions:** The higher prevalence of thyroid disorders among patients with type-2 diabetes mellitus highlights the importance of screening type-2 diabetes mellitus patients for the presence of thyroid disorders.

**Keywords:** Hyperthyroidism; thyroid disorders; Type-2 diabetes mellitus

## INTRODUCTION

The type-2 diabetes mellitus and thyroid disorders are the two most common endocrine disorders all over the world and they mutually affect each other.<sup>1</sup> Patients with type-2 diabetes mellitus are at higher risk of suffering from various thyroid dysfunctions due to interaction between insulin, glycemic control, and thyroid hormone at cellular, biochemical and genetic level.<sup>2-4</sup>

In various studies, the prevalence of thyroid disorders is found to be higher than normal in patients of type-2 diabetes mellitus.<sup>5</sup> Diabetes mellitus is associated with the increased risk of cardiovascular problems.<sup>6</sup> This increase in the cardiovascular risk is amplified by the co-existence of thyroid disease.<sup>5</sup> So, understanding the mutual relation between the type 2 diabetes mellitus and thyroid disorders is key for the optimal management of patients and prevention of complications.<sup>1</sup>

This study aims to identify the prevalence and various

spectrums of thyroid disorders in patients with type 2 diabetes mellitus in Nepal.

## METHODS

This was a cross-sectional, hospital-based study, conducted among 204 type-2 diabetes mellitus patients attending internal medicine department of Shree Birendra Hospital, located in Kathmandu district of Nepal. The Institutional Review Committee (IRC) of Nepalese Army Institute of Health Sciences (NAIHS - IRC, Ref.No. 245) had approved our protocol prior to starting the study. All adult patients of age 18 years and above with type 2 diabetes mellitus, giving written consent, were enrolled in the study, irrespective of their glucose control and the modality of the treatment they were receiving. Patients with type-1 diabetes mellitus, gestational diabetes mellitus, diabetic ketoacidosis, hyperglycemic hyperosmotic state, chronic kidney disease, pancreatitis, fever in the last seven days, proven thyroid disorders and receiving treatment for

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same and, those who refused to give written consent were excluded from this study.

Data collection was completed in one year duration from 1<sup>st</sup> March, 2019 till 28<sup>th</sup> February, 2020. Non-probability purposive method of sampling was used for the collection of data. The sample size was calculated on the basis of prevalence of thyroid disorders in patients with diabetes, 2.2 to 17% as reported in a study done by Papazafropoulou et.al.<sup>7</sup> Taking the prevalence of 15%, at confidence interval of 95% and allowable error at 5%, the sample size was calculated as minimum of 204.

Data was collected on self-designed semi-structured pro forma, which included questions related to demographic variables and relevant clinical history. Following interview by researcher, participants were subjected to the blood tests required for the study. Fasting blood sugar (FBS), post prandial blood sugar (PPBS), hemoglobin A1c (HbA1c), free triiodothyronine (fT<sub>3</sub>), free thyroxine (fT<sub>4</sub>), thyroid-stimulating hormone (TSH) was measured in the blood sample. HbA1c assay was performed by commercially available Axis (Nycocard), a GNSP (National Glycohemoglobin Standardization Program) Certified and DCCT (Diabetes Control and Complications Trial) Standardized Assay. Thyroid function test was performed by using commercially available kit in fully automated immunoassay analyzer-ADVIA Centaur CP Immunoassay System. Blood sugar levels were measured by enzymatic method (GOD-POD Glucose Oxidase Peroxidase method) using Sysmex BX4000 Automated Chemistry Analyzer. The reference range for fT<sub>3</sub>, fT<sub>4</sub>, and TSH used in this study was 2.30-4.20 pg/mL, 0.89-1.76 ng/dL, and 0.35-5.50 µIU/mL respectively. In this study, euthyroidism was defined as having all fT<sub>3</sub>, fT<sub>4</sub>, and TSH within the reference range. Subclinical hypothyroidism was defined as having raised TSH level with normal fT<sub>4</sub> level. Overt hypothyroidism was defined as having raised TSH level with low fT<sub>4</sub> level. Subclinical hyperthyroidism was defined as having decreased TSH level with normal fT<sub>4</sub> level. Overt hyperthyroidism was defined as having decreased TSH level with raised fT<sub>4</sub> level. In this study, patients with HbA1c level ≤ 7% were considered to have good glycemic control, and those with HbA1c >7% were considered to have poor glycemic control. Similarly, those participants who have had diabetes for ≥10 years were considered as having long duration of diabetes.

Data was entered in Statistical Package for Social Science for Windows (SPSS) version 21 for statistical analysis. Descriptive statistics were calculated using frequency and percentage for qualitative variables, and mean and standard deviation for quantitative variables. Chi-square test was used to compare categorical variables. A 95%

confidence interval was used in this study and p-value of < 0.05 was considered to be statistically significant.

## RESULT

A total of 204 patients with type-2 diabetes mellitus were enrolled in the study. Among 204 patients, 56.4% (115) were male and 43.6 % (89) were females. The mean age of the patients was 60.94 ± 12.252 years, mean BMI was 24.09 ± 4.251 kg/m<sup>2</sup>, and mean duration of the diabetes was 8.149 ± 7.396 years.

Of the total 204 patients enrolled in the study, 72.06% (147) had normal thyroid status, and 27.94% (57) had thyroid dysfunction. Among the 27.94% (57) patients with thyroid dysfunction, hypothyroidism was seen 22.55% (46) and hyperthyroidism in 5.39% (11). On further stratifying the spectrum of thyroid dysfunctions, subclinical hypothyroidism occurred in 14.71% (30), overt hypothyroidism in 7.84% (16), subclinical hyperthyroidism in 5.39% (11), and overt hyperthyroidism in 0% (0). So, subclinical hypothyroidism was the most common spectrum of thyroid dysfunction in the patients enrolled in this study (Figure 1).

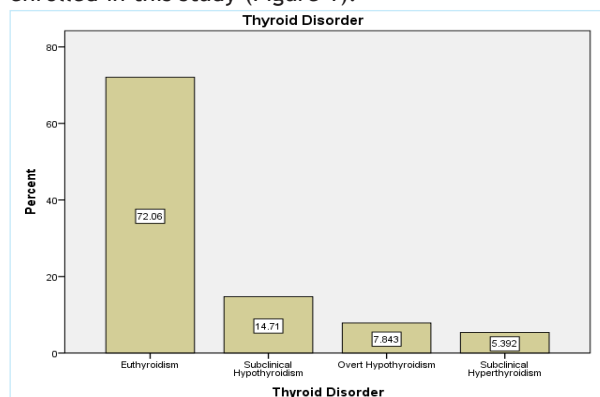


Figure 1. Bar diagram showing spectrum of thyroid dysfunction in patients with T2DM.

Among 115 males included in the study, 73.91% (85) were euthyroid, 13.04% (15) had subclinical hypothyroidism, 7.83% (9) had overt hypothyroidism, 5.22% (6) had subclinical hyperthyroidism and none had overt hyperthyroidism. Similarly, among total 89 females in study population, 69.66% (62) were euthyroid, 16.85% (15) had subclinical hypothyroidism, 7.87% (7) had overt hypothyroidism, 5.62% (5) had subclinical hyperthyroidism and none had overt hyperthyroidism. Female patients had more thyroid dysfunctions in comparison to the male patients. The most common thyroid disorder was subclinical hypothyroidism in both males and females. However, on comparing the thyroid status of male and female patients using the Pearson Chi-Square test, there was no significant difference in

thyroid status among the male and female patients with type-2 diabetes mellitus ( $p = 0.502$ ) (Table 1).

**Table 1. Relationship of gender and thyroid status.**

		Thyroid Status		Total
		Euthyroid	Thyroid Dysfunction	
Gender	Male	85	30	115
	Female	62	27	89
Total		147	57	204

Pearson Chi-Square test:  $df-1$ ;  $p$  value- 0.502

On stratifying patients with type-2 diabetes mellitus into various age groups, those patients falling under the age group of 60-69 years had highest prevalence of thyroid dysfunction. On comparing thyroid status of various age groups using Chi-Square test,  $p$  value was 0.838, suggesting that there was no significant difference in the status of thyroid dysfunction between various age groups (Table 2).

**Table 2. Frequency of thyroid status by age groups.**

		Thyroid Status		Total
		Euthyroid	Thyroid Dysfunction	
Age Groups	20-29	1	0	1
	30-39	9	1	10
	40-49	13	5	18
	50-59	38	17	55
	60-69	50	18	68
	70-79	27	13	40
	80-89	9	3	12
	Total		147	57

Pearson Chi-Square test:  $df-6$ ;  $p$  value-0.838

On comparing the thyroid status among type-2 diabetes patients based on their duration of diabetes, patients with duration of diabetes more than or equal to 10 years were significantly more likely to have thyroid dysfunction in comparison to those patients with duration of diabetes less than 10 years ( $p = 0.025$ ) (Table 3).

**Table 3. Comparison of thyroid status with diabetes duration more or less than 10 years.**

		Thyroid Status		Total
		Euthyroid	Thyroid Dysfunction	
Duration more or less than 10 years	Up to 10 years	102	30	132
	More than 10 years	45	27	72
Total		147	57	204

$df-1$ ;  $p$  value-0.025

In this study, type-2 diabetes mellitus patients with poor glycemic control,  $HbA1c \geq 7\%$ , had significantly higher prevalence of thyroid dysfunction in comparison to patients with good glycemic control ( $p=0.002$ ) (Table 4).

**Table 4. Comparison of glycemic control and thyroid dysfunction**

		Thyroid Status		Total
		Euthyroid	Thyroid Dysfunction	
HbA1c Classification	$HbA1c < 7$	60	10	70
	$HbA1c \geq 7$	87	47	134
Total		147	57	204

$df-1$ ;  $p$  value-0.002

## DISCUSSION

Thyroid dysfunction and type-2 diabetes mellitus are the two most common endocrine disorders all over the world, and studies show that they mutually affect each other.<sup>1</sup> In various studies the prevalence of thyroid disorders is found to be higher than normal in patients of diabetes mellitus.<sup>5</sup> Diabetes mellitus is associated with the increased risk of cardiovascular problems.<sup>6</sup> This increase in the cardiovascular risk is amplified by the co-existence of thyroid disease.<sup>5</sup> So, understanding the mutual relation between the type 2 diabetes mellitus and thyroid disorders is key for the optimal management of patients and prevention of complications.<sup>1</sup>

This study was performed in 204 type-2 diabetes mellitus patients to identify the prevalence of thyroid disorders in type-2 diabetes, to analyze various spectrum of the thyroid disease in type-2 diabetes, and to find the association of factors related to type-2 diabetes, such duration of disease, and glycemic control, with thyroid disorders.

In this study the prevalence of thyroid dysfunction was 27.94% among patients with type-2 diabetes mellitus. This prevalence is in agreement with previous studies showing association between type-2 diabetes mellitus and thyroid dysfunction.<sup>1, 8-17</sup> In three studies done in Nepal, the prevalence of thyroid disorder was almost similar to this study.<sup>14, 17, 18</sup> A study done by Khatiwada et al. in Nepal in 2015, found that the prevalence thyroid dysfunction was 35.41% in type 2 diabetes patients.<sup>14</sup> Similarly in another study done in Nepal by Bhusal et al., the prevalence of thyroid disorder in diabetes mellitus was 35%.<sup>17</sup> A study done by Demitrost in India showed 31.2 % prevalence of thyroid dysfunction in diabetic patients, which is similar to this study.<sup>8</sup> Similarly, in the studies done by Diez et al.<sup>9</sup> and Witting et al.<sup>10</sup> in type-

2 diabetic patients, the prevalence of thyroid disorders was 32.4% and 27.3% respectively. Also, in the studies done by Zhu et al.<sup>12</sup>, Al-Geffari et al.<sup>13</sup>, Uppal et al.<sup>1</sup>, Telwani et al.<sup>15</sup>, Ozair et al.<sup>16</sup>, the prevalence of thyroid dysfunction on type 2 diabetes patients was 23.79%, 28.5%, 27.8%, 24.5%, 29%, and 28% respectively, which is similar to the result of this study.

In this study the most common thyroid disorder was hypothyroidism. Of the total patients enrolled in this study 22.55% had hypothyroidism. Among them subclinical hypothyroidism was 14.71% and overt hypothyroidism was 7.84%. So, among all thyroid disorders subclinical hypothyroidism was the most common thyroid dysfunction in type-2 diabetes mellitus. A study done by Demitrost et al. showed similar result, in which hypothyroidism was the most common thyroid disorder in type-2 diabetes and subclinical hypothyroidism was most common thyroid dysfunction among hypothyroid patients.<sup>8</sup> In another study done by Diez et al., hypothyroidism was the most common thyroid disorder in patients with type 2 diabetes mellitus, where hypothyroidism was present in 25.8% of the diabetic patients.<sup>9</sup> In a study done by Witting et al., hypothyroidism was the most common thyroid disorder, like in this study.<sup>10</sup> Radaideh et al. in their study also found subclinical hypothyroidism to be the most common thyroid disorder in type 2 diabetes patients.<sup>19</sup> Similarly Centeno et al., in their study also found hypothyroidism as the most common thyroid disorder in type 2 diabetes.<sup>11</sup> In addition to the above mentioned studies, the studies done by Zhu et al.<sup>12</sup>, Palma et al.<sup>20</sup>, Al-Geffari et al.<sup>13</sup>, Alsolami et al.<sup>21</sup>, Nair et al.<sup>22</sup>, Uppal et al.<sup>1</sup>, Telwani et al.<sup>15</sup>, Subekti et al.<sup>23</sup>, Ozair et al.<sup>16</sup>, Jali et al.<sup>24</sup> concluded that hypothyroidism was the most common thyroid disorder in patients with type-2 diabetes mellitus. A study done in Kathmandu also showed that hypothyroidism was most common thyroid disorder among type 2 diabetes patients.<sup>17</sup> In agreement with our study, the studies done by Perros et al.<sup>25</sup>, Radaideh et al.<sup>19</sup>, Centeno et al.<sup>11</sup>, Palma et al.<sup>20</sup>, Telwani et al.<sup>15</sup>, Subekti et al.<sup>23</sup>, Ozair et al.<sup>16</sup>, Bhusal et al.<sup>17</sup> demonstrated that subclinical hypothyroidism was the most common thyroid disorder in patients with type-2 diabetes mellitus. Hence, the result of our study showing hypothyroidism and among it subclinical hypothyroidism as the most common thyroid problem in type 2 diabetes mellitus is consistent with the result of the various studies.

In this study, female patients had more thyroid disorders than male patients. Out of the 115 males 26.09% had thyroid dysfunction, and among females 30.34% had thyroid dysfunction. However, on comparing the thyroid

disorders among sex categories, the association was not significant. In both males and females, hypothyroidism was the most common disorder with subclinical hypothyroidism accounting for the most cases. In the studies done by Demitrost et al.<sup>8</sup>, Papazafiropoulou et al.<sup>7</sup>, Witting et al.<sup>10</sup>, Distiller et al.<sup>26</sup>, Uppal et al.<sup>1</sup>, Telwani et al.<sup>15</sup>, Ozair et al.<sup>16</sup>, Jali et al.<sup>24</sup> prevalence of thyroid disorders was found to be high in females than in males, which is in agreement with the result of this study. The studies performed by Al-Geffari et al.<sup>13</sup> and Ogbonna et al.<sup>3</sup> established female gender as the risk factor for the thyroid dysfunction. Ogbonna et al. also showed that female patients with diabetes had 3.8 times more chance of developing thyroid dysfunction in comparison to the males.<sup>3</sup> Similar to this study, in two studies done in Nepal, the prevalence of thyroid disorder was found to be more in females than in males.<sup>14, 18</sup>

In this study, the prevalence of thyroid dysfunction among type-2 diabetes patients was found to be highest (31.58%) in the age group of 60-69 years but there was no statistically significant difference in thyroid dysfunction among various age groups (p value 0.838). The result of our study is in agreement with the various studies done by other authors. In a study by Jali et al. the prevalence of thyroid dysfunction was highest in patients more than 50 years of age.<sup>24</sup> Similarly in the study by Demitrost et al., the prevalence of thyroid dysfunction was found to be high in those with age more than 45 years.<sup>8</sup> Al-Geffari et al. found that the mean age of diabetic patients with thyroid dysfunction was 59.3±9.9.<sup>13</sup> In a study done in India, 79.3% of patients with diabetes with thyroid dysfunction had age ≥ 50 years.<sup>15</sup> The increase in the prevalence of the thyroid with increasing age might be due to the undetected diabetes for a longer duration in many elderly patients, and also due to the increase in insulin resistance and decline in beta cell function with increasing age.<sup>24</sup>

In this study, the longer duration of the type-2 diabetes was associated with the higher prevalence of the thyroid disorders. The prevalence of thyroid dysfunction, in this study, was significantly more in patients who have had type-2 diabetes more than 10 years (p value 0.025), suggesting that the longer duration of the diabetes increases the chances of developing thyroid dysfunction. The result of the present study is similar to the study done by Al-Geffari et al. who showed that the patients with duration of diabetes more than 10 years had significant increased risk of having thyroid dysfunction.<sup>13</sup> Similarly, Telwani et al. found that the prevalence of thyroid disorders was more in type 2 diabetes patients with duration of the diabetes more than 5 years, which

is in agreement with the result of our study.<sup>15</sup> Also, Ogbonna et al. reported that the duration of diabetes more than 5 years was a risk factor for thyroid disorders.<sup>3</sup> The association of the longer duration of type 2 diabetes with the increase in the presence of thyroid dysfunction might be due to the fact that the chronically increased blood sugar level impairs the peripheral deiodination of  $T_4$  to  $T_3$  leading to the thyroid dysfunction.<sup>3</sup> In contrast to our study, studies done by Jali et al.<sup>24</sup>, Ozair et al.<sup>16</sup>, and Diez et al.<sup>9</sup> didn't find any significant relationship between the thyroid dysfunction and the duration of the type-2 diabetes.

In this study, poor glycemic control,  $HbA1c \geq 7\%$ , was associated with significantly increased thyroid dysfunction in type-2 diabetes patients (p value 0.002). Jali et al. also reported that the poorly controlled type-2 diabetes increased the risk of developing thyroid dysfunction compared to well controlled type-2 diabetes.<sup>24</sup> In another study, it was observed that type-2 diabetes patients with high  $HbA1c$  level were 4.3 times more likely to develop thyroid dysfunction in comparison to their counterparts with  $HbA1c$  level  $<7\%$ .<sup>3</sup> This increase in the prevalence of the thyroid dysfunction with poor glycemic control might be due to the adverse effect of chronically increased blood sugar on hypothalamo-pituitary axis where it decreases or stops the nocturnal peak of TSH.<sup>3</sup> In contrast to our study, Diez et al.<sup>9</sup> and Telwani et al.<sup>15</sup> didn't find any significant association between glycemic control and the prevalence of the thyroid disorders. More studies might be necessary to find the actual relation between the glycemic control and the thyroid hormone status.

This study was conducted in a sample of modest size in a single center, so the effects of modest sample size should be considered while generalizing the results.

## CONCLUSIONS

This study showed high prevalence of thyroid dysfunction in the patients with type-2 diabetes mellitus. Subclinical hypothyroidism was the most common type of thyroid dysfunction. The prevalence of thyroid dysfunction was high among females and elderly patients with type-2 diabetes mellitus. The presence of thyroid disorder increased with the increase in the duration of the type-2 diabetes and with the poor glycemic control. This study highlights the importance of screening type-2 diabetes mellitus patients for presence of thyroid dysfunction. Further studies exploring the association of thyroid dysfunction and type-2 diabetes mellitus are necessary for better understanding in future.

## CONFLICT OF INTEREST

The authors declare no conflict of interest

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