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A Comparative Study of Thyroid Function in Patients of Type 2 Diabetes Mellitus without Nephropathy and Type 2 Diabetes Mellitus With Nephropathy.

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ABSTRACT

Background: Diabetes Mellitus is an important health problem affecting major population worldwide. It is characterized by absolute or relative deficiency in insulin secretion and/or insulin action associated with chronic hyperglycemia and disturbances of carbohydrate, lipid and protein metabolism. The prevalence of type II diabetes mellitus for all age groups worldwide was estimated to be 2.8% in 2000 and likely to increase to 4.4% in 2030. The number of people with diabetes is projected to rise from 285 million adults in 2010 to 439 million adults in 2030. In India, it is estimated that presently 31.7 million individuals are affected by this deadly disease, which are likely to increase to 79.4 million by the year 2030. Diabetes patients with nephropathy have higher prevalence of thyroid disorder than type 2 DM without nephropathy which may have an influence on diabetic management. Diabetic women are frequently affected than men and hypothyroidism is more common than thyrotoxicosis. **Methods:** In our study 100 patients with type 2 DM attending Guru Nanak Dev hospital attached to GMC Amritsar were recruited. These patients were divided into two groups of 50 patients each. Group 1 consisted of patients of type 2 DM without nephropathy and group 2 consisted of patients of type 2 DM with nephropathy. **Results:** Out of 100 patients thyroid dysfunction was more prevalent in diabetic nephropathy group as compared to diabetic without nephropathy group. P-value for thyroid dysfunction in diabetic nephropathy was statistically significant. In our study we found a statistically significant correlation between TSH and serum insulin levels in patients with diabetic and diabetic nephropathy. Higher prevalence of thyroid dysfunction like low T3 syndrome and subclinical hypothyroidism was found in women as compared to men. **Conclusion:** Routine assessment of thyroid hormone level in addition to other biochemical parameters in the early stage of diabetes and diabetes nephropathy will help in the management of those patients who are difficult to manage.

Keywords: Thyroid function, Diabetes Mellitus type 2 and Diabetic Nephropathy.

INTRODUCTION

Diabetes Mellitus is an important health problem affecting major population worldwide. It is characterized by absolute or relative deficiency in insulin secretion and/or insulin action associated with chronic hyperglycemia and disturbances of carbohydrate, lipid and protein metabolism.[1]

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It is associated with various microvascular complications like nephropathy, retinopathy, neuropathy etc which increase the morbidity and mortality in diabetic patients. Diabetic Nephropathy, a major microvascular complication of type II DM, is an important cause of chronic kidney disease. It results from interaction between hemodynamic and metabolic factors.[2] A higher proportion of individuals with type 2 diabetes are found to have diabetic nephropathy shortly after the diagnosis of their diabetes, because of the unnoticed presence of diabetes for many years before its diagnosis. Subclinical hypothyroidism is the most prevalent form of thyroid dysfunction in type 2 DM.[3] Nephropathy affects both hypothalamus-pituitary-thyroid axis and thyroid hormone peripheral metabolism.[4] Uraemia influences the function and

size of thyroid.[5] Serum TSH concentrations are usually normal or elevated in nephropathy, but its response to its releasing hormone i.e. thyroid releasing hormone is generally low.[5]

MATERIALS AND METHODS

In the present study, the patients were divided into two groups of 50 patients each one without diabetic nephropathy and the other with diabetic nephropathy. The study includes one hundred patients of either sex in age group of 40-70 years diagnosed to be a case of type 2 DM attending OPD/ admitted in emergency and medical wards of Guru Nanak Dev Hospital/Government Medical College, Amritsar. After obtaining informed consent, the patients were subjected to detailed history, clinical examination and various lab investigations. Lab investigations consisted of thyroid function tests, blood sugar fasting and postprandial, HbA1c, serum insulin levels, serum creatinine, and urinary albumin creatinine ratio.

Inclusion Criteria:
1. Age 40-70 years
2. Type 2 DM with or without nephropathy.
Exclusion Criteria:
3. Known case of thyroid disorder (hypothyroidism or hyperthyroidism).
4. Age less than 40years.
5. Age more than 70 years.
6. Patients on long term glucocorticoids, thyroxin or anti-thyroid drugs.
7. Other known autoimmune disorders.
8. Human immunodeficiency virus (HIV+ve) patients
9. Hepatitis B & Hepatitis C positive patients.

Collection & Processing of Blood Sample:
Blood samples were collected from all the 100 subjects. Patients were kept on overnight fast for at least eight hours before blood collection. From each subject 5ml of venous blood sample was drawn by aseptic technique.

RESULTS

Among 100 diabetic patients recruited in the study, out of 50 were without diabetic nephropathy and 50 with diabetic nephropathy. Mean age of patient with and without nephropathy was almost same i.e. 56.86 ± 9.68 and 56.94 ± 8.51 years respectively. Hypertension was more prevalent in diabetic nephropathy as compared to without diabetic nephropathy with significant p value of 0.002 (significant). The mean value of T3 was 1.09±0.45 in group 1 and 0.96±0.53 in group 2. So T3 was decreased in group 2 as compared to group 1. The mean value of TSH was 3.55±1.54 in group 1 and 4.46±4.22 in group 2. So TSH was increased in group 2 as compared to group 1. TSH was found to be increased with increasing values of insulin in both the groups which suggest that correlation of insulin resistance with subclinical hypo-thyroidism (high levels of TSH). In diabetic patients both with and without diabetic nephropathy. TSH was found to be increasing trend with increased values of serum creatinine in diabetic nephropathy. TSH levels in type 2 diabetic nephropathy increases with increase in urinary albumin creatinine ratio, which shows that serum TSH level (subclinical hypothyroidism) was an independent risk factor of albuminuria.

Association of thyroid dysfunction with prevalence of diabetic nephropathy:
To investigate the association of thyroid dysfunction with diabetic nephropathy, the prevalence of thyroid dysfunction in group 1 was compared with that of group 2. Group 1 there were 44(88%) euthyroid patients, 2(4%) low T3 syndrome, 4(8%) subclinical hypothyroidism and no overt hypothyroidism patient. In group 2 there were 26(52%) euthyroid patients, 11(22%) low T3 syndrome, 12 (24%) subclinical hypothyroidism and 1(2%) overt hypothyroidism patient respectively. P value was significant ,so the prevalence of thyroid disorder was found to be higher in group 2. The prevalence of thyroid dysfunction was found to be more in females as compared to males in both the groups.

Table 1: Thyroid Dysfunction.

Thyroid Dysfunction	Group I (n=50)		Group II (n=50)		Total
	No.	%	No.	%	
Normal	44	88.0	26	52.0	70
Low T3 Syndrome	2	4.0	11	22.0	13
Subclinical Hypothyroidism	4	8.0	12	24.0	16
Overt Hypothyroidism	-	-	1	2.0	1
Total	50	100.0	50	100.0	100

$x^2 = 15.859$; df = 3; p = 0.001; Significant

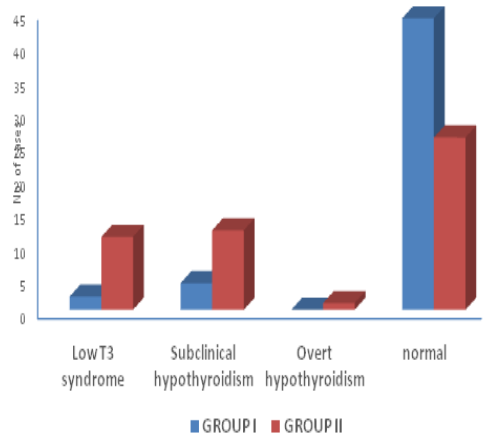

Figure 2: Number of patients of Low T3, Subclinical & Overt Hypothyroidism.

Table 2: Insulin Distribution.

Insulin micro IU/ml	n	Group I (n=50)			n	Group II (n=50)		
		T3	T4	TSH		T3	T4	TSH
25-50	43	1.1±.454	7.2±2.06	3.2±.84	41	0.9±.5	7.6±1.89	3.3±2.3
50-75	6	1.00±0.378	6.5± 2.1	5.8±3.2	9	1.1±0.52	7.2±1.08	9.8±6.6
>75	1	0.3± 0	4.9± 0	4.3±	0	-	-	-
p-value		0.194	0.461	<.01		0.267	0.568	<.01

Table 3: Correlation of Various Biochemical Parameters with Thyroid Function Test Abnormalities in Group I.

Group I	FBS	PPBG	HBA1c	Serum insulin level	T3	T4	TSH
Low T3 syndrome							
Female (n=2)							
Range	134-312	336-344	6.0-6.9	32.9-98	0.2-0.3	4.9-5.8	3.4-4.3
Mean	223±125	340±5.6	6.45±0.6	65.45±40	0.25±0.07	5.35 ±0.63	3.85±0.636
Sub clinical hypothyroidism							
Male(n=1)							
Range							
Mean	210	249	7.5	56	0.5	4.8	8.7
Female (n=3)							
Range	128-311	201-354	7.4-7.6	50.5-53.0	0.8-1.6	4.4-9.6	5.5-9.4
Mean	209±93	287±78.2	7.5±0.1	51.36±1.4	1.2± 0.40	7.5±2.7	7.2±1.9

Table 4: Correlation of Various Biochemical Parameters with Thyroid Function Test Abnormalities In Group II.

Group II	FBS	PPBG	HBA1c	Serum insulin level	S.creatinine	Urinary ACR	T3	T4	TSH
Low T3 syndrome									
Male(n=4)									
Range	137-318	244-354	6.5-12.4	26.2-39.0	1.2-2.98	31-148	0.1-0.4	5.6-10.0	2.4-4.09
Mean	225.5± 101	317.75± 50.45	8.75± 2.5	32.37± 5.23	2.12± 0.73	108.5± 53.2	0.25± 0.12	7.3± 1.97	3.055± 0.723
Female (n=7)									
Range	153-321	204-345	6.2-8.2	29.6-37.6	1.8-3.8	43-468	0.1-0.4	5.8-9.2	0.86-3.19
Mean	238± 70	299± 46.5	7.2± 0.73	32.75± 2.76	2.9± 0.74	209± 138.9	0.24± 0.09	7.64± 1.27	2.06± 0.81
Sub clinical hypothyroidism									
Male(n=3)									
Range	143-300	245-321	7.1-8.8	46.62	1.93-2.5	51-186	1.3-1.5	6.5-9.3	8.35-9.98
Mean	245.33± 88.692	289± 39.552	8.1± 0.88	55 ±8.22	2.27± 0.30	138.3± 75.7	1.4± 0.1	7.66± 1.45	9.0± 0.85
Female(n=9)									
Range	148-334	208-378	7.2-10.2	39-65.4	2-8.2	122-382	0.6-1.9	4.9-8.2	5.3-10
Mean	260.4± 69.53	306 ±50.46	8.0± 0.98	51.04± 7.88	3.25± 1.9	195± 85.5	1.18± 0.41	6.7± 1.07	7.9± 1.84
Over hypothyroidism									
Female (n=1)									
Mean	150	228	7.9	53	6.4	225	0.1	6.4	27

DISCUSSION

In our study 100 patients with type 2 DM attending Guru Nanak Dev hospital attached to GMC Amritsar were recruited. These patients were divided into two groups of 50 patients each. Group 1 consisted of patients of type 2 DM without nephropathy and group 2 consisted of patients of type 2 DM with nephropathy.

In our study in group 1 there were 14(28%) males, 36(72%) females, mean age of patients was 56.86±9.689 and 21(42%) were hypertensive. In group 2 there were 16(32%) males, 34(68%) females, mean age of patients was 56.94±8.51 and 36(72%) patients were hypertensive. Similar study done by Furukawa et al in 2014 found that mean age of patients in group 1 was 61.6±10.7 years and 60% were male. In group 2 mean age of patients was 61±11.5 years and 72.4% were male.[6] In present study we observed that in group 1 there were 21 (42%) hypertensive and in group 2, 36(72%) patients were hypertensive. There were more hypertensive patients in group 2 as compare to group 1 with significant p value (0.002). There was no significant

p-value found regarding age and sex (p-value 0.965, 0.0663 respectively.)

Similar study done by Furukawa et al[6] in year 2014 found that in group 1 there were 38.9% hypertensive while in group 2, 72.4% were hypertensive with significant p value regarding hypertension and age (p –value 0.001,0 and 0.014 respectively) but insignificant p value regarding gender distribution (p =0.458). Result of above study similar to our study except age and gender distribution. In a study done by Mansournia el al in year 2016 showed that 155 patients has fasting sugar blood level mean value was 142.1 in diabetics without nephropathy while 105 patients had fasting blood sugar mean value was 150.4 in diabetic nephropathy patients. In present study, mean value of T3 in group 1 was 1.096±0.45 ng/ml as compare to 0.964±0.53 ng/ml in group 2 indicating decreasing trend of T3 in group 2 which was comparable to study done by Srinidhi et al[7]. The mean value of TSH in group 1 was 3.55±1.54 microIU/ml as compared to 4.46±4.22 microIU/ml in group 2 showing increasing trend with Type 2 DM nephropathy. Similar finding was shown in study done by Srinidhi et al.[7] We observe that in group 1, patients in the serum insulin range 25-50 micro IU/ml were 43 in number with mean values of T3 (ng/ml), T4 (Micro gm/dl) and TSH (Micro IU/ml) were 1.1±0.45, 7.2±2.06 and 3.2±0.84 respectively. Patients with serum insulin range 50-75 microIU/ml were 6 in number with mean values of T3, T4 and TSH were 1.00±0.37, 6.5±2.1 and 5.8±3.2 respectively. Patients with serum insulin range>75 microIU/ml was 1 in number with mean values of T3, T4 and TSH were 0.3, 4.9 and 4.3 respectively. In group 2, patients in serum insulin range 25-50 were 41 in number with mean values of T3 (ng/ml), T4 (Microgm/dl) and TSH (MicroIU/ml) were 0.9±0.5, 7.6±1.89 and 3.3±2.3 respectively. Patients with serum insulin range 50-75 microIU/ml were 9 in number with mean values of T3 (ng/ml), T4 (Microgm/dl) and TSH (MicroIU/ml) were 1.1±0.52, 7.2±1.08 and 9.8±6.6 respectively. No patient found in serum insulin levels >75 micro IU/ml. P value of TSH was significant in both the groups i.e. p <0.01. In a study done by Singh et al[8] in year 2010 found that TSH levels were positively correlated with serum insulin levels with significant P value<0.01. In one another study done by Rajeswari et al[9] in year 2015 found that TSH levels were positively correlated with insulin in patients with subclinical hypothyroidism (SCH). There study indicated that insulin resistance was present not only in overt hypothyroidism but it was significantly present in subclinical hypothyroidism also. In present study in group 2 mean value of TSH level was 4.4±4.2 micro IU/ml in 30-299 mg/g urinary albumin creatinine ratio (UACR) range while it was 4.86±4.5 microIU/ml in >300 mg/g UACR range, which shows the increasing trend of TSH with increase in UACR levels. Similarly Furukawa et. al.[6] in year 2014 in his study showed higher incidence of subclinical hypothyroidism (high levels of TSH) in type 2 diabetic nephropathy group as compared to type 2 diabetes without nephropathy group. In present study in group 1 out of 50 patients, 2(4%) had low T3 syndrome, 4(8%) had subclinical hypothyroidism while in group 2, 11 (22%) had low T3 syndrome, 12(24%) had subclinical hypothyroidism and 1 (2%) had overt hypothyroidism. The overall P-value for thyroid dysfunction in diabetic nephropathy i. e. Group 2 was significant with p value =0.001. Similarly a study done by Miulescuet al[10] in 2014 year found that higher incidence of thyroid dysfunction in type 2 DN as compared to type 2 DM without nephropathy in the form of Low T3 syndrome (23.80% vs. 0.00%), subclinical hypothyroidism (23.80% vs. 9.52%) and overt hypothyroidism (8.69% vs. 4.76%). In a study done by Furukawa et al[6] in year 2014 the prevalence of subclinical hypothyroidism was 20.7% in diabetic nephropathy group while 8.7% in diabetic without nephropathy group.

In another study done by Mansournia et. al.[11] in year 2016 showed incidence of subclinical hypothyroidism in diabetic nephropathy was 29% as compare to 17% in without diabetic nephropathy group while in present study there were 24% patients in diabetic nephropathy group had subclinical hypothyroidism and 8% in type 2 diabetes without nephropathy group.

CONCLUSION

In our study 100 patients with type 2 DM attending Guru Nanak Dev hospital attached to GMC Amritsar were recruited. These patients were divided into two groups of 50 patients each. Group 1 consisted of patients of type 2 DM without nephropathy and group 2 consisted of patients of type 2 DM with nephropathy. Thyroid dysfunctions in the form of low T3 syndrome, subclinical hypothyroidism and overt hypothyroidism were more commonly found in type 2 DM nephropathy than type 2 DM without nephropathy.

1. Among type 2 DM nephropathy patients 11(22%) had low T3 syndrome, 12 (24%) had subclinical hypothyroidism and 1 (2%) had overt hypothyroidism while in type 2 DM without nephropathy patients 2 (4%) had low T3 syndrome and 4(8%) had subclinical hypothyroidism signifying that thyroid dysfunction was more prevalent in diabetic nephropathy group.
2. In group 1 there were 14 male patients from which 13 normal, no low T3 syndrome, 1 subclinical hypothyroidism and no overt hypothyroidism patient and there were 36 female patients among them 31 were normal, 2 low T3 syndrome, 3 subclinical hypothyroidism and no overt hypothyroidism

patient. In group 2 there were 16 male patients from which 9 normal, 4 low T3 syndrome, 3 subclinical hypothyroidism and no overt hypothyroidism patient. There were 34 female patients in group 2 from which 17 normal, 7 low T3 syndrome, 9 subclinical hypothyroidism and 1 overt hypothyroidism.

3. In present study thyroid dysfunctions were more prevalent in females in type 2 DM nephropathy patients as compared to type 2 DM without nephropathy patients. We observed that TSH levels were positively correlated with insulin levels with p value statistically significant ($p<0.05$). In present study serum TSH levels in type 2 diabetic nephropathy increases with increase in urinary albumin creatinine ratio. In our study hypertension has positive correlation ($p<0.05$) with type 2 diabetic nephropathy patients. Insulin resistance correlate positively with hypothyroidism status. Hence it will be good practice to screen people for presence of sub clinical hypothyroidism (high levels of TSH.) and insulin resistance, so that early detection and prompt intervention if required. TSH levels in type 2 diabetic nephropathy increases with increase in urinary albumin creatinine ratio, which shows that serum TSH level (subclinical hypothyroidism) was an independent risk factor of albuminuria. There is need for the routine assay of thyroid hormones in type 2 diabetics and diabetic nephropathy in order to improve the quality of life and reduce the morbidity. In the present study we have observed that the abnormal thyroid hormone levels among type 2 diabetics without nephropathy and type 2 diabetics with nephropathy. Failure to recognize the presence of abnormal thyroid function may be a primary cause of poor management of diabetes mellitus. Therefore there is need for the routine assay of thyroid hormones in type 2 diabetics and diabetic nephropathy in order to improve the quality of life and reduce the morbidity.

REFERENCES

1. Tiwari AK, Roa JM. Diabetes mellitus and multiple therapeutic approaches of phytochemicals. Present status and future prospectus. Current Science. 2002; 83(1): 30–38.
2. Navarro Gonzalez JF, Mora Fernandez C, De Fuentes MM, Garcia Perez J. Inflammatory molecules and pathways in the pathogenesis of diabetic nephropathy. Nature Reviews Nephrology. 2011; 7: 327–40.
3. Cannaris GJ, Manowitz NR, Mayor G. The Colorado thyroid disease prevalence study. Arch intern Med. 2000; 160; 526-534.
4. Kar P, Hirani A, Allen MJ. Acute renal failure in a hypothyroid patient with rhabdomyolysis. Clinical Nephrology. 2003; 60: 428–9.
5. Kaptein EM. Thyroid hormone metabolism and thyroid diseases in chronic renal failure. Endocrine Reviews. 1996; 17: 45–63.
6. Furukawa S, Yamamoto S, Todo Y, Maruyama K, Miyake T, Ueda T, et al. Association between subclinical hypothyroidism and diabetic nephropathy in patients with type 2 diabetes mellitus. Endocr J. 2014; 61(10): 1011-8.
7. Rai S, JA. Kumar, K. Prajna. Thyroid function in type 2 diabetes mellitus and in diabetic nephropathy. Journal of clinical and Diagnostic Research. 2013; 7(8): 1583-1585.
8. Singh BM, Goswami B, Mallika V. Association between insulin resistance and hypothyroidism in females attending a tertiary care hospital. Indian journal of clinical biochemistry. 2010; 25: 141-5.
9. Rajeshwari G, Gopal PS, Srinivas PS, Suresh E. Study of insulin level in hypothyroidism patients. Int J Med Sci. 2015; 3: 2000-3.
10. Danciulescu Miulescu R, Neemtu MC, Margina D, Poiana C, Paun DL. Association between thyroid dysfunction and chronic kidney disease. Romanian journal of Diabetes Nutrition and Metabolic Diseases. 2014; 1(21): 37-42.
11. Mansournia M, Riyahi S, Tofangchiha MA, Mansournia MA, Riahi M, Heidari Z et al. Subclinical hypothyroidism and diabetic nephropathy in Iranian patients with type 2 diabetes. J Endocrinol Invest. 2016.

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