(International Print/Online Journal)

SJIF IMPACT FACTOR: 5.565
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume 6, Issue 3 , Page No: 90-100
May-June 2023

IJMSCR

A Comparative Study of TSH and Anti-TPO in Type 2 Diabetic and non-Diabetic Patients

Dr. Amrita Tripathi[1]*, Dr. Kalbe Jawad[2], Dr. Ajai Kumar[3], Dr. Granth Kumar[4], Dr. Dhiraj Kumar Srivastava[5], Dr. Pradeep Sharma[6], Dr. Santosh Kumar Dubey[7]

[1,7]MBBS & Post Graduate Junior Resident,[2]PhD, Professor and Head,[3]MD, Assistant Professor, [4,5]MD, Professor,[6]PhD, Professor

[1,2,3,6]Department of Biochemistry, [4]Department of Medicine, [5]Department of Community Medicine, [7]Department of Head and Neck UPUMS, Saifai, Etawah, Uttar Pradesh, India

***Corresponding Author:**
Dr. Amrita Tripathi
MBBS, Post Graduate Junior Resident, Department of Biochemistry, UPUMS, Saifai, Etawah, Uttar Pradesh, India

Type of Publication: Original Research Paper
Conflicts of Interest: Nil

Abstract

Introduction:

Diabetic patients have a higher prevalence of thyroid disorders than the non-diabetic population, this may influence diabetic management. In this study, we aimed to compare TSH and Anti-TPO in diabetics and non-diabetics.

Materials and Methods:

This case-control study was conducted among 200 study participants aged > 30 years. Participants were subjected to bio-chemical analysis including, fasting blood sugar, post-prandial blood sugar, glycated hemoglobin, TSH and anti-TPO antibodies.

Observations:

Among diabetic population, TSH and anti-TPO antibody levels showed significantly low positive correlation with FBS (0.430 and 0.443, respectively). Similarly, TSH and anti-TPO antibody levels showed significantly low positive correlation with HbA1c (0.362 and 0.314, respectively). Among non-diabetic population no significant correlation was found between thyroid parameters and diabetic profile.

Conclusions:

Prevalence of thyroid dysfunction is more common among type 2 diabetes mellitus patients than in general population. There is significant low positive correlation between FBS, PPBS, and HbA1c level with TSH and anti-TPO.

Keywords: Anti-Thyroid peroxidase antibody, Thyroid stimulating hormone, Type-2 Diabetes mellitus

Introduction

Diabetes mellitus (DM) is a leading cause of health-related problems and death in different populations worldwide.[1] According to World Health Organization (WHO), the worldwide prevalence of diabetes projected to grow up to 366 million or more by 2030.[2] India has 65.1 million people with type 2 diabetes and it will increase to 109 million by 2030.[3]

Thyroid disorders are common in the general population and it is common for an individual to be affected by both thyroid disease and diabetes.[4] DM appears to influence thyroid function in two sites; firstly, at the level of hypothalamic control of TSH release; Secondly, at peripheral tissue by converting T4 to T3. Hyperglycemia causes reduction in hepatic concentration of T4-5 deiodinase, low serum

concentration of T3, raised levels of reverse T3 and low, normal, or high level of T4. Thyroid hormone regulate metabolism and diabetes can alter metabolism. [5] Studies done at various geographical region have reported the prevalence of thyroid dysfunction among diabetic patients between 2.2 to 29%[6,7]. This variability of prevalence is usually due to different diagnostic criteria of thyroid disorder, degree of iodine intake in different region, different sensitivities of the TSH assays and the large population diversity.[8]

It is seen that many diabetic patients may remain asymptomatic especially in subclinical hypothyroidism. Hence, screening of diabetic patients for thyroid disorder is justified for early detection. Anti-thyroid peroxidase antibodies (Anti-TPO) and/or anti-thyroglobulin antibodies (Anti-TG) can be detected long before the changes in TSH and thyroid hormone levels occur. Thus, determination of these antibodies might be useful for early diagnosis of the disease before abnormal thyroid-stimulating hormone (TSH) values develop. [9]

There is a continuing interest in the association between thyroid disorders in diabetes mellitus type 2. Furthermore, on extensive search of literature we found no major studies have been conducted to compare and correlate serum insulin levels and total tri-iodothyronine (T3), thyroxine (T4), thyroid stimulating hormone (TSH) levels in type 2 diabetes mellitus patients. Data on comparison and correlation of the glycated hemoglobin (HbA1c) levels and total T3, T4, TSH levels and role of anti-TPO in type 2 diabetes mellitus patients is also scanty.[10]

So, the present study aimed to compare TSH and Anti –TPO level in Diabetic and non-Diabetic and to determine the prevalence of thyroid dysfunction and its correlation with Diabetes Mellitus. This study demonstrates the importance of recognition of this interdependent relationship between thyroid disease and diabetes which in turn will help and guide clinicians on the optimal screening and management of these conditions.

Methodology:

A Hospital-Based Case-Control Study was conducted in UPUMS, Saifai, Etawah U.P. to find out serum TSH and Anti-TPO in Diabetic and non- Diabetic patients in the Rural area of Western Uttar Pradesh.

Sample Size: Minimum Sample size was calculated considering the prevalence (p) of 13%. Therefore, the study was carried out of 100 cases and 100 control

CASES: Group I: Patients with Type 2 DM attending Medicine In & Out - Patient Department (Age > 30 years)

CONTROL: Group II same age and sex- matched healthy individuals were taken as Controls.

Inclusion Criteria:

1) All patients with type 2 diabetes aged >30 years.

2) Above patients irrespective of glucose control and treatment.

Exclusion Criteria:

1. Type 1 DM
2. Gestational DM
3. Steroid induced diabetes
4. Known thyroid disorder.
5. Physiological stress
6. Sepsis
7. Neurological and psychological illness
8. Malignancy
9. Other Co-morbidities.

Study Methods

The individuals satisfying all inclusion criteria were selected for the study and those with at least any one exclusion criteria were not invited to participate in the study. They were recruited for the study as per clearance from the Ethical Committee of the Institute. Informed written consent was taken from all the participants at the time of recruitment. A pre-tested and pre-validated printed questionnaire was used to collect information on the social, demographical, occupational, dietary and medical history. The FBS, PPBS, HbA1c, TSH, ANTI-TPO were performed for both cases and control.

Biochemical Analysis of serum

Following biochemical parameters were analyzed during study:

Volume 6, Issue 3; May-June 2023; Page No 90-100

(A) ESTIMATION OF PLASMA GLUCOSE: Based on the Principle of Enzymatic colorimetric Trinder end point (GOD-POD) method.

(B) ESTIMATION OF HbA1c: Based on the Principle of Ion exchange high performance liquid chromatography (HPLC).

(**C) ESTIMATION OF SERUM Anti-TPO and TSH-** Based on the Principle of Chemiluminescent Immunoassay (CLIA).

The laboratory reference ranges for parameters were as follows-

HbA1c	3.0-5.7%
Fasting blood sugar	70-110 mg/dl
Post prandial blood sugar	70-140 mg/dl
TSH	0.4-4.94 μIU/mL
Subclinical hypothyroid	TSH>4.94 μIU/mL
Anti-TPO	<35.0 IU/mL

Statistical analysis: Statistical analysis was performed using statistical software SPSS version 23(or latest version). The data was expressed as arithmetic mean with Standard

Deviation; P<0.05 was considered as statistically significant. By applying chi-square, student's unpaired t-test and logistic regression between two groups, wherever applicable. P<0.05 was considered as a statistically significant.

Observations:

The study sample included 100 type 2 diabetes patients as cases and 100 non-diabetic healthy persons as controls. Following were the observations.

Table 1: Distribution of study participants based on Socio-demographic characteristics with diabetic profile, Thyroid Stimulating Hormone (TSH) levels, and Anti- Thyroid peroxidase (TPO) levels (N=200)

Variables		**Age**		**Gender**	
		< 60 years	≥ 60 years	Female	Male
Diabetes	**Present (n=100)**	66 (66.0)	34 (34.0)	49 (49.0)	51 (51.0)
	Absent (n=100)	71 (71.0)	29 (29.0)	48 (48.0)	52 (52.0)
	p-value	0.447*		0.887*	
TSH	**Normal (n=155)**	104 (67.1)	51 (32.9)	74 (47.7)	81 (52.3)
	Abnormal (n=45)	33 (73.3)	12 (26.7)	23 (51.1)	22 (48.9)
	p-value	0.428*		0.691*	
Anti-TPO	**Normal (n=168)**	113 (67.3)	55 (32.7)	78 (46.4)	90 (53.6)
	Abnormal (n=32)	24 (75.0)	8 (25.0)	19 (59.4)	13 (40.6)
	p-value	0.388*		0.176*	

*Chi-square test

Volume 6, Issue 3; May-June 2023; Page No 90-100

There is no significant difference in the age and gender distribution among the diabetic and non-diabetic study participants, patients with normal or abnormal TSH levels and patients with normal or abnormal anti-TPO levels. [Table 1].

Table 2: Diabetic profile of the diabetic and non-diabetic participants (N=200)

		Diabetic (n=100) Frequency (%)	Non-diabetic (n=100) Frequency (%)	p-value
FBS (mg/dl)	**Mean ± SD**	147.28 ± 14.72	77.05 ± 8.75	<0.001#
	Up to 99	0 (0.0)	100 (100.0)	<0.001$
	100 to 125	0 (0.0)	0 (0.0)	
	± 126	100 (100.0)	0 (0.0)	
PPBS (mg/dl)	**Mean ± SD**	267.84 ± 26.87	115.76 ± 10.12	<0.001#
	< 140	0 (0.0)	99 (99.0)	<0.001$
	140 to 199	0 (0.0)	1 (1.0)	
	≥ 200	100 (100.0)	0 (0.0)	
HbA1c (%)	**Mean ± SD**	9.38 ± 2.81	4.92 ± 0.46	<0.001#
	< 5.7	0 (0.0)	100 (100.0)	<0.001$
	5.7 to 6.4	0 (0.0)	0 (0.0)	
	> 6.4	100 (100.0)	0 (0.0)	
TSH µIU/mL	Mean ± SD	14.45 ± 30.20	2.25 ± 1.11	<0.001#
	Normal (0.40-4.94)	61 (61.0)	94 (94.0)	<0.001*
	Abnormal (< 0.40 or >4.94)	39 (39.0)	6 (6.0)	
Anti-TPO (units/mL)	Mean ± SD	150.65 ± 274.18	0.85 ± 1.61	0.000#
	Normal (≤35)	68 (68.0)	100 (100.0)	<0.001$
	Abnormal (>35)	32 (32.0)	0 (0.0)	

#Independent samples t-test, FBS (Fasting Blood Sugar), PPBS (Post Prandial Blood Sugar), #Independent samples t-test, *Chi-square Test, $Fisher`s Exact Test, TSH (Thyroid Stimulating Hormone), Anti TPO (Thyroid Peroxidase) antibody

There was 39 percent prevalence of abnormal TSH level among the diabetics, and abnormal levels of anti-TPO antibodies was found in 32 percent of the diabetic patients. Levels of both the parameters was significantly higher among the diabetic group compared to the non-diabetic group. The mean TSH levels were higher among

Volume 6, Issue 3; May-June 2023; Page No 90-100

the diabetic group (14.45 µIU/mL) compared to the non-diabetic group (2.25 µIU/mL). Similarly, the mean anti-TPO antibody level among the diabetic group (150.65 units/mL) was significantly higher that the non-diabetic group (0.85 units/mL). [Table 2].

Table 3: Correlation of thyroid dysfunction with diabetes mellitus

Diabetic profile		**Thyroid dysfunction**	
		TSH (µIU/mL)	**Anti-TPO Antibody(units/mL)**
Total population	FBS	0.376*	0.458*
	PPBS	0.291*	0.355*
	HbA1c	0.434*	0.462*
Diabetic population	FBS	0.430*	0.443*
	PPBS	0.106	0.022
	HbA1c	0.362*	0.314*
Non-diabetic population	FBS	0.065	0.060
	PPBS	0.002	0.114
	HbA1c	-0.071	-0.011

*Pearson`s Correlation is significant at 0.01 level (2-tailed)

Among diabetic population, TSH and anti-TPO antibody levels showed significantly low positive correlation with FBS (0.430 and 0.443, respectively). Similarly, TSH and anti-TPO antibody levels showed significantly low positive correlation with HbA1c (0.362 and 0.314, respectively). Among non-diabetic population no significant correlation was found between thyroid parameters and diabetic profile. [Table 3].

Figure 1: Correlation of TSH levels with Fasting Blood Sugar

(a) Diabetic population (b) non-diabetic population

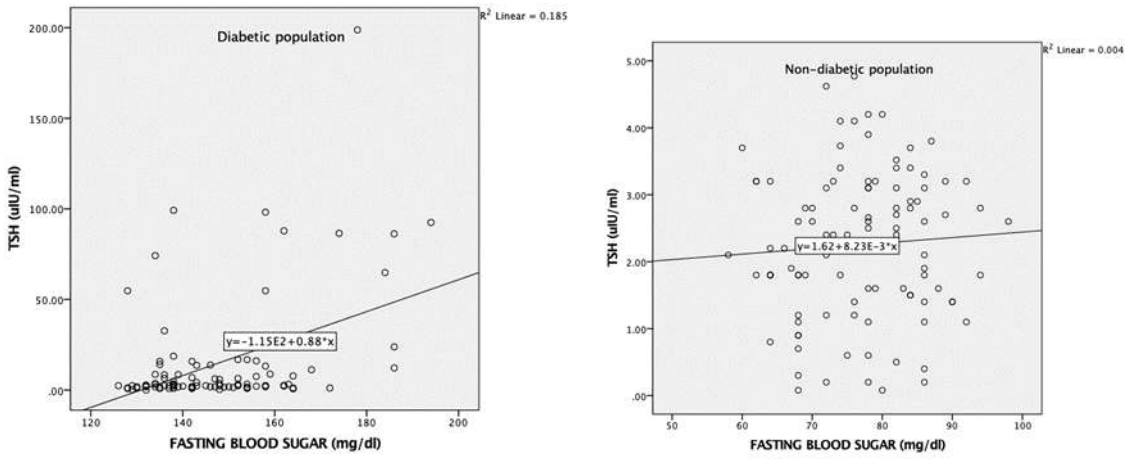


Figure 1 showed that among diabetic population one unit change in the FBS level is correlated with 0.88 units change in TSH, whereas, among non-diabetic population, only 0.4 percent of the variance could be predicted by the model.

Volume 6, Issue 3; May-June 2023; Page No 90-100

Figure 2: Correlation of TSH levels with Post-Prandial Blood Sugar

(a) Diabetic population (b) non-diabetic population

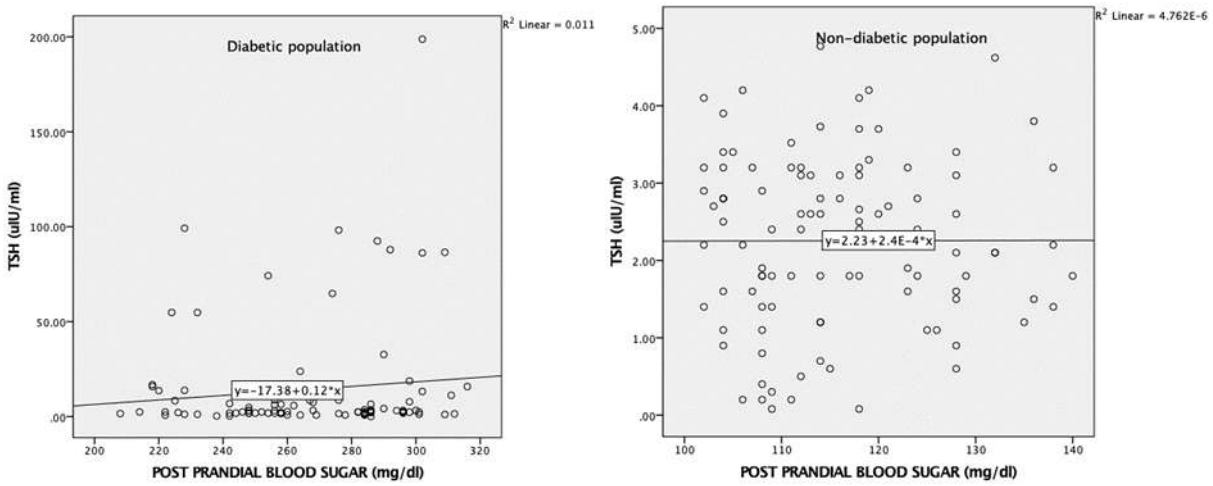


Figure 2 showed that among diabetic population one unit change in the PPBS level is correlated with 0.12 units change in TSH, whereas, among non-diabetic population, there was no correlation between the two variables.

Figure 3: Correlation of TSH levels with Glycosylated hemoglobin (HbA1c)

(a) Diabetic population (b) non-diabetic population

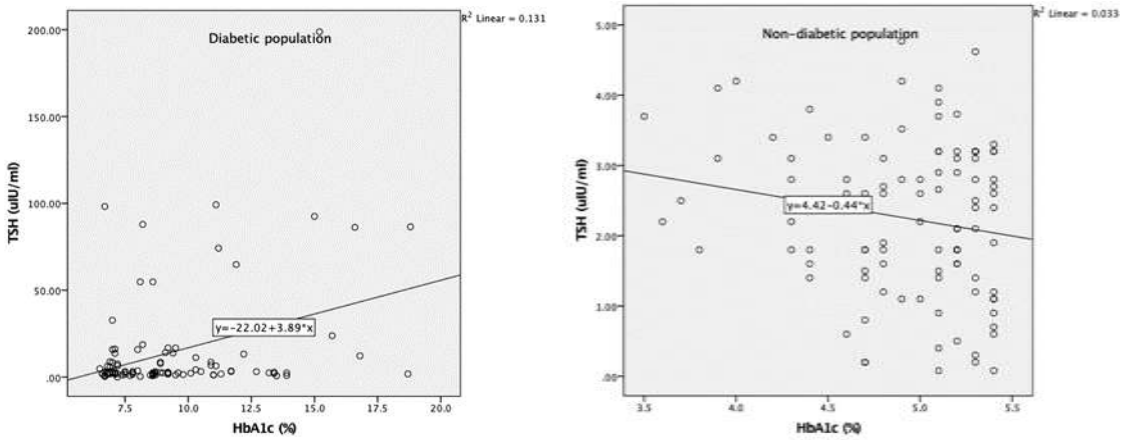


Figure 3 showed that among diabetic population one unit change in the HbA1c level is correlated with 3.89 units change in TSH, whereas, among non-diabetic population, the unit change in Hba1c correlated negatively with 0.44 units change in TSH.

Volume 6, Issue 3; May-June 2023; Page No 90-100

Figure 4: Correlation of Anti-TPO antibody levels with Fasting Blood Sugar

(a) Diabetic population (b) non-diabetic population

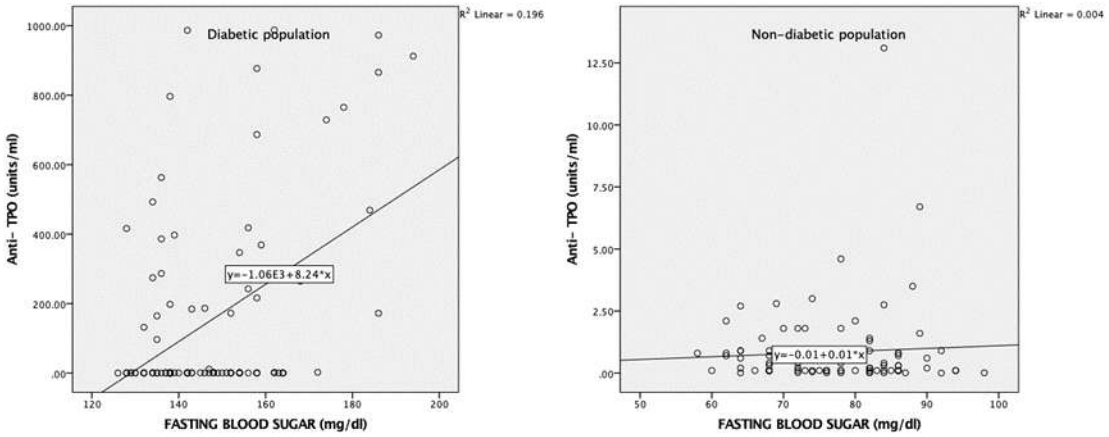


Figure 4 showed that among diabetic population one unit change in the FBS level is correlated with 8.24 units change in anti- TPO antibodies, whereas, among non-diabetic population, the unit change in the FBS levels have negligible correlation with units change in anti-TPO antibodies.

Figure 5: Correlation of Anti-TPO antibody levels with Post-Prandial Blood Sugar

(a) Diabetic population (b) non-diabetic population

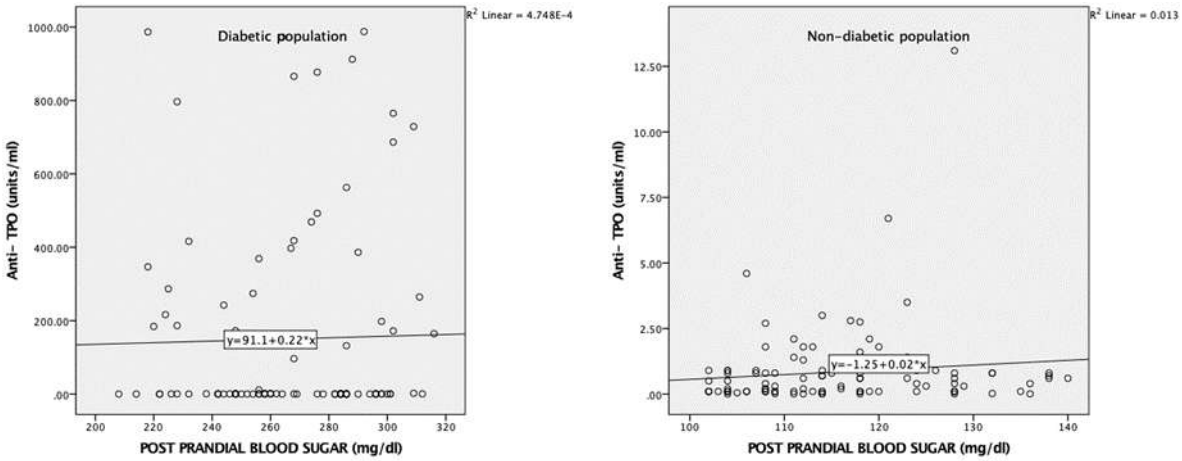
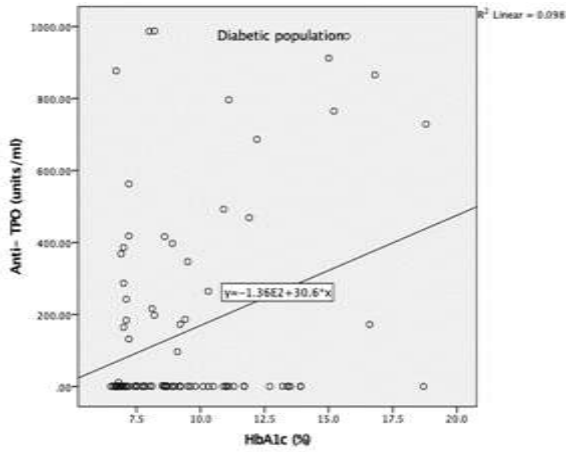


Figure 10 showed that among diabetic and non-diabetic population there is negligible correlation of anti-TPO antibodies level and post-prandial blood sugar.

Volume 6, Issue 3; May-June 2023; Page No 90-100

Figure 6: Correlation of Anti- TPO antibody levels with Glycated hemoglobin (HbA1c)

(a) Diabetic population



(b) non-diabetic population

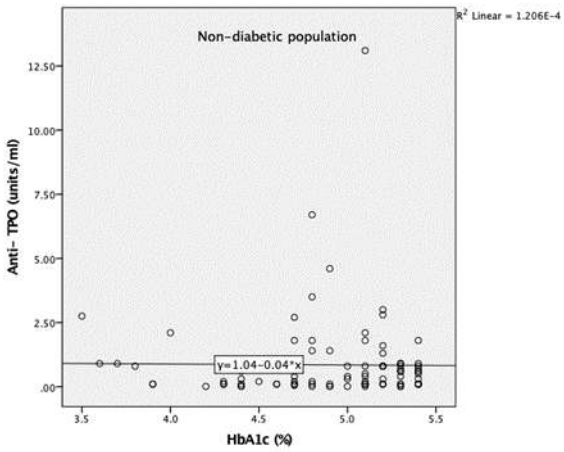


Figure 6 showed that among diabetic population one unit change in the HbA1c level is correlated with 30.6 units change in anti-TPO antibodies, whereas, among non-diabetic population, there is no correlation between the anti-TPO antibodies levels and HbA1c.

Discussion:

The present case-control study was carried out to compare TSH and Anti-TPO level in diabetic and non-diabetic patients without any evidence of clinical thyroid disease.

Socio-demographic characteristics of the study participants:

Age distribution:

The present study shows the preponderance of diabetes in middle aged population (<60 years. This observation was similar to WHO report which predicts that in India and developing countries the highest increase would occur in the age group of 45-65 year of age group. [11] Kapur et al.[12] also reported that maximum number of cases were diagnosed between 40 and 59 years of age with no significant difference between diabetic and non-diabetic groups.

Among the patients with abnormal TSH levels, around three-fourths (73.3%) of the diabetic patients were aged less than 60 years. Vondra et al.[13] in his study found that thyroid diseases in diabetic patients is 2-3 times higher than in nondiabetic subjects and it raises with age.

Gender:

In the present study 51 percent of the diabetic population were males. This may be attributed to the small sample size of the study. This observation was similar to Jali et al.[14] and Flatau E et al.[15] who reported that diabetes was more prevalent in men than in women. This is in contrast to Michalek AM et al.[16] who reported that prevalence of diabetes among women was higher than in men. Vondra et.al in his study found that thyroid diseases is strongly influenced by female gender and autoimmune diabetes.

In the present study 51.1 percent of the study participants with abnormal TSH levels were females compared to the participants with normal TSH levels (47.7% were females). Compared between patients with normal and abnormal TSH levels, this difference is however, statistically not significant. Celani MF et al.[17] , Michalek AM et al.[**Error! Bookmark not defined.**] and Abdel-Rahman et al.[18] in their study found that the prevalence of thyroid dysfunction was significantly higher in the females than in the males and there is a significant correlation between female gender and altered thyroid profile.

Diabetic profile of the study participants:

The mean fasting blood sugar among diabetics was significantly higher compared to the non-diabetic study participants. Similarly, post prandial blood sugar was significantly higher among the diabetics, than the non-diabetic study participants. Sanad et al.[19] also reported the similar findings in their study, where the mean FBS level among the diabetic group

Volume 6, Issue 3; May-June 2023; Page No 90-100

was 143.88 mg/dl compared to 94.15 mg/dl among the non-diabetic group. The mean HbA1c in the present study was 9.38 percent among the diabetics, similar to the findings reported by Paolo fumelli in his study among diabetic patients found that all the mean HbA1c was greater than eight percent.[20]

Abnormal Thyroid Profile:

There was 39 percent prevalence of abnormal TSH level among the diabetics and abnormal levels of anti-TPO antibodies was found in 32 percent of the diabetic patients. Our study findings regarding the prevalence of thyroid dysfunction in diabetes mellitus is proximate to the prevalence seen in the studies done by Celani et al.[**Error! Bookmark not defined.**] (31%), Vikram et al.[21] (30%) and Gurjeet singh et al.[22] (30%). The present study found the prevalence of abnormal TSH levels among non-diabetic as 6%, similar to the findings of Abdel-Rahman et al.,[**Error! Bookmark not defined.**] Smithson MJ et al.,[7] and Akbar DH et al.,[23] who in their study found that the prevalence of thyroid disease among non-diabetic control group was 6.6%, 6.6% and 7%, respectively. This shows that the thyroid function abnormalities are common in diabetic populations and their prevalence vary from 12.5% to 31.4% in previous studies. The previous literature also suggests that the prevalence of abnormal TSH levels among non-diabetic persons ranged between 3.8 to 7 percent. The presence of altered thyroid profile in diabetic patients may be due to the fact that firstly in euthyroid individuals with diabetes mellitus, the serum T3 levels, basal TSH levels and TSH response to thyrotropin releasing hormone (TRH) may all be strongly influenced by the glycemic status[24].Secondly, poorly controlled diabetes may also result in impaired TSH response to TRH or loss of normal nocturnal TSH peak.[25] Thirdly, it may be related to older age of the type 2 DM patients.[26]

Correlation of TSH and Anti-TPO levels among diabetic and non-diabetic patients:

Levels of both the parameters was significantly higher among the diabetic group compared to the non-diabetic group. The mean TSH and anti-TPO levels were significantly higher among the diabetic group (14.45 µIU/ml and 150.65 IU/ml, respectively) compared to the non-diabetic group (2.25 µIU/ml and 0.85 IU/ml, respectively). In term of simple correlation coefficients (person's correlation coefficients), there were various significant levels for the extracted responding coefficients between a study parameter which indicated meaningful interactions. Among diabetic population, TSH and anti-TPO antibody levels showed significantly low positive correlation with FBS (0.430 and 0.443, respectively). Similarly, TSH and anti-TPO antibody levels showed significantly low positive correlation with HbA1c (0.362 and 0.314, respectively). Among non-diabetic population no significant correlation was found between thyroid parameters and diabetic profile. Celani MF et al.[**Error! Bookmark not defined.**] in their study among 91 diabetic patients with altered thyroid profile found that TSH level in serum decreased significantly with fall in HbA1c level. Vamshidhar IS et al.[27] in their study also reported a positive correlation of TSH with FBS and HbA1c. However, the findings are in contrast to the studies by Parr JH et al.[28] and Chubb et al[28] who found no correlation between changes in free thyroid hormone concentrations and HbA1c level among diabetic population.

Limitations:

1. Study population was small.
2. Associated thyroid autoimmunity was not evaluated due to constraints. So, it was not able to refine the spectrum of thyroid dysfunction in type 2 diabetics.
3. This was a single center study and was not externally validated.
4. Some types of selection bias may have occurred because these patients are already under medical care.
5. A long follow up study was needed to assess the natural history of subclinical thyroid dysfunction and its effect on various diabetic parameters could not be assessed.

Conclusion:

1. Prevalence of thyroid dysfunction is more common among type 2 diabetes mellitus patients than in general population.
2. Prevalence of thyroid dysfunction in patients with type 2 diabetes mellitus is higher in females than in males
3. There is significant low positive correlation between FBS, PPBS, and HbA1c level with TSH and anti-TPO.

Volume 6, Issue 3; May-June 2023; Page No 90-100

4. Routine screening for thyroid dysfunction in type 2 diabetes mellitus patients may be justified especially in females because the progression to overt thyroid dysfunction is associated with significant morbidity including the adverse effects on glycemic control and hence the disease progression.

Acknowledgement: The author, Dr Amrita Tripathi expresses her gratitude and wish to thank Shivanand Maurya, technician for his immense support in carrying out this Research. The authors, also thankful to the patients who participated in the study.

References

1. Faghilimnai S, Hashemipour M, Kelishadi, B. Lipid profile of children with type 1 diabetes compared to controls. ARYA. J. 2006; 2(1): 36 - 38.
2. World Health Organization. Report of WHO study group. World Health Organ Tech Rep S. 1985;727
3. Zimmat P, Alberti KG, Shaw J. Global and societal implications of the diabetes epidemic. Nature. 2000; 414 (6865): 782-7.
4. Gray RS, Irvine WJ, Clarke BF. Screening for thyroid dysfunction in diabetics. Br Med J. 1979; 2 (6202): 1439.
5. Shah SN. Thyroid disease in diabetes mellitus. J Assoc Physicians India. 2007;32(12):1057- 1059.
6. Perros P, Mc Cremona RJ, Shaw G, Frier BM. Frequency of thyroid dysfunction in diabetic patients: value of annual screening. Diabet Med. 1995; 12 (7): 622-627.
7. Smithson MJ. Screening for thyroid dysfunction in a community population of diabetic patients. Diabet Med.1998; 15 (2): 148-150.
8. Udiong CEJ, Udoh AE , Etukudoh, ME. Evaluation of thyroid function in diabetes mellitus in Calabar , Nigeria. Indian Journal of Clinical Biochemistry 2007; 22(2) :74- 78.
9. Bárová H., Perusicová J., Hill M., Sterzl I., Vondra K., Masek Z., Anti-GAD-positive patients with type 1 diabetes mellitus have higher prevalence of autoimmune thyroiditis than anti-GAD-negative patients with type 1 and type 2 diabetes mellitus, Physiol Res., 2004, 53, 279-286
10. Uppal V, Vij C, Bedi GK, Vij A, Banerjee BD. Thyroid Disorders in Patients of Type 2 Diabetes Mellitus. Indian J Clin Biochem. 2013 Oct; 28(4): 336–341.
11. Wild S, Rogli G, Green A. Global prevalence of diabetes estimates for the year 2000 and projection for 2030. Diabetes Care, 2004; 27: 1047-53.
12. Kapur A., Snehlatha C., Ramchandran A., Vijay V., Mohan V., Das A.K., Rao PV., Yajnik CS., Prasanna Kumar K.M., Jyotsna Nair: High prevalence of diabetes and impaired glucose tolerance in India. National Urban diabetes survey. Diabetologia 2001; Vol. 44: 1094 –1101.
13. Vondra K, Vrbikova J, Dyorakova K. Thyroid gland diseases in adult patients with diabetes mellitus. Minerva Endocrinol. 2005 Dec;30(4):217-36.
14. Jali MV, Mohan V, Ramchandran A, Snehlatha C and Viswanathan M; High Prevalence of diabetes in an Urban population in South India. BMJ Sept 1988; Vol. 297: p- 587-590.
15. Flatau E, Trougouboff P, Kaufman N, Reichman N, Luboshitzky R. Prevalence of hypothyroidism and diabetes mellitus in elderly kibbutz members. Eur J Epidemiol. 2000;16(1, January):43-6. doi: 10.1023/a:1007688113450, PMID 10780341.
16. Michalek AM, Mahoney MC, Calebaugh D. Hypothyroidism and diabetes mellitus in an American Indian population. J Fam Pract. 2000 July;49(7):638-40. PMID 10923575.
17. Celani MF, Bonati ME, Stucci N. prevalence of abnormal thyrotrophin concentrations measured by a sensitive assay in type 2 diabetes mellitus. Diabetes Res. 1994;27(1):15-25. PMID 7648793.
18. Radaideh AR, Nusier MK, Amari FL, Bateiha AE, El-Khateeb MS, Naser AS et al. Thyroid dysfunction in patients with type 2 diabetes mellitus in Jordan. Saudi Med J. 2004 Aug;25(8):1046-50. PMID 15322596.
19. Sanad B Al–A Araji, Taufeek F Rasen, Reiam A. Kadhum. Biochemical Study on Anti Thyroid Peroxidase in Type 2 Diabetic patients with thyroid disorders. Baghdad Science Journal. 2016 Dec. 4;13(4):0753. Available from: https://bsj.uobaghdad.edu.iq/index.php/BSJ/article/view/2316
20. Paolo Fumelli, Silvia Natalucci, Massimo Boemi. One and two compartment minimal models detect similar alterations of glucose metabolism indexes

Volume 6, Issue 3; May-June 2023; Page No 90-100

in hypertension. Metabolism.Volume 49;12: 1529-1536
21. Vikhe VB, Kanitkar SA, Tamakuwala KK, Gaikwad AN, Kalyan M, Agarwal RR et al. thyroid dysfunction in patients with type 2 diabetes mellitus at tertiary care centre. national journal of medical research print ISSN: 2249 4995 | eISSN: 2277 8810.
22. Singh G et al Evaluation of Thyroid Dysfunction Among type 2 diabetic Punjabi Population advances in bio search,2011;Vol.2:2.
23. Akbar DH, Ahmed MM, Al-Mughales J. Thyroid dysfunction and thyroid autoimmunity in Saudi type 2diabetics. Acta Diabetol. 2006;43(1):14-8. doi: 10.1007/s00592-006-0204-8, PMID 16710644.
24. Schlienger JL, Anceau A, Chabrier G, North ML, Stephan F. Effect of diabetic control on the level of circulating thyroid hormones. Diabetologia. 1982;22;486-8
25. Coiro V, Volpi R, Marchesi C, Capretti L, Speroni G, Caffarri G, et al. Influence of residual C-peptide secretion on nocturnal serum TSH peak in well-controlled diabetic patients. Clin Endocrinol (Oxf). 1997;47(3):305-10. doi: 10.1046/j.1365-2265.1997.2501063.x, PMID 9373451.
26. Chubb SA, Davis WA, Inman Z, Davis DME. Prevalence and progression of subclinical hypothyroidism in women with type 2 diabetes: the Fremantle Diabetes Study. Clin Endocrinol (Oxf). 2005Apr;62(4):480-6.
27. Vamshidhar IS, Rani SSS. A Study of Association of Thyroid Dysfunctions in Patients with Type 2 Diabetes Mellitus. Maedica (Bucur). 2020 Jun;15(2):169-173. doi: 10.26574/maedica.2020.15.2.169. PMID: 32952680; PMCID: PMC7482697.
28. Parr JH. The effect of long-term metabolic control on free thyroid hormone levels in diabetics during insulin treatment. Ann Clin Biochem. 1987 Sep;24(5):466-9.

Volume 6, Issue 3; May-June 2023; Page No 90-100