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Is Thyroid Dysfunction higher in Elderly Patients with Long Duration of Diabetes Mellitus (LDDM) Need for Thyroid Diagnosis

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Abstract

Aims: To identify in both gender, the association between ages, duration of diabetes, and thyroid markers like TPO Ag, and Tg Ab.

Methods: 584 patients were selected for the study. Patient demographic details such as age, gender, geographic area, and duration of diabetes were recorded. Diabetic markers and thyroid markers were done and recorded.

Statistical significance was found using SPSS version 20.0. Frequencies with percentages and Fisher's Exact test were used to compare the predictors like Tg Ag, and TPO Ag with the age of the patients and duration of diabetes. A p-value of <0.05 was considered statistically significant.

Results: Out of 584 patients 200 patients were diabetic, and 384 were non-diabetic, a higher number of 340 (58.2%) of selected patients lived in the valley. Females 386 (66.1%), housewives/unemployed were in higher numbers in the study population. The mean age was 46 ± 16.44. The intake of iodine was 100%. 315 (53.9%), patients were found positive for thyroid hormones, among them TPO Ab positive was 103 (32.7%), Tg Ab was 169 (53.7%), and both TPO Ab & Tg Ab were 43 (13.6%)

Females showed high positivity for both TPO Ab and Tg Ab (0.0469). TPO Ab was equal in the age group of ≤ 29 years (0.0021) but was higher in females than males in all age groups. Tg Ab was higher in30 – 49 years of females (R^2-0.318), ≤ 29, 50 – 69 years in males (R^2-0.483), Both TPO Ab and Tg Ab were higher in females than males (0.0265).

The diabetic patients with 5 – 10 years duration of diabetes found higher positivity for TPO Ab and Tg Ab in both genders. As the duration of diabetes increased, Tg Ab positivity increased (R^2-0.02), whereas in females Tg Ab gradually decreased as the duration of diabetes increased (R^2-0.618). TPO Ab positivity also increased in females as the duration of diabetes increased to 5 – 10 years, and gradually decreased (R^2-0.473). In males, TPO Ag positivity increased as the duration of diabetes

increased significantly from 5 – 20 years (R^2-0.132) time of diabetes.

Conclusions: As thyroid dysfunction is under-diagnosed, un-reported, and does not with specific tool to differentiate thyroid cancer, and other thyroid dysfunction, this study served as active surveillance to identify thyroid markers positivity in the non-diabetic population, and diabetic population, the association between vital factors such as age, duration of diabetes, and thyroid markers positivity.

Keywords: Thyroid Dysfunction, Thymoglobulin, Thyro peroxidase, Diabetes Mellitus, Thyrotropin Releasing Hormone, Thyroid hyper trophy, Tri-iodothyronine.

Introduction

Thyroid disorders and diabetes mellitus are combined to place a heavy strain on medical science and the population of the world[1]. The growing number of diabetics in our nation and the critical causal connection between diabetes mellitus and thyroid dysfunction are tightly related[2]. Studies have shown that thyroid issues are more common in those with diabetes mellitus and vice versa[3].

The mechanism relating overt and subclinical hypothyroidism to type 2 diabetes and metabolic syndrome are complex and facts hidden[4]. Evaluating the current state of knowledge on the central and peripheral control of thyroid hormone on food intake, glucose and lipid metabolism in target tissues such as the liver, white and brown adipose tissue, pancreatic cells, and skeletal muscle are still a few questions to answer clearly[5].

Thyroid hypertrophy (diffuse or nodular), symptoms of thyroid hormone deficiency (hypo thyroidism), symptoms of thyroid hormone excess (thyro toxicosis), or none of the above (the sub clinical state) are possible presentations of thyroid dysfunction[6].

Thyroid gland dysfunction, pituitary gland dysfunction (which generates TSH), and hypo thalamic dysfunction (which controls the pituitary gland via Thyrotropin Releasing Hormone (TRH) are all causes of imbalanced thyroid hormone production[7].

Food intake, resting energy expenditure, and thermogenesis are all impacted, and as a result, patients with Thyroid Dysfunction (TD) may experience metabolic changes[8]. Tri-iodothyronine (T3) affects meta bolism and thermogenesis by controlling (i) appetite, (ii) appetite-related transcription factors, and (iii) glucose and lipid metabolism and oxidation[9].

Instead, information about general nutritional status, circadian rhythms, and stress are integrated by the combination of central nutritional state and hormonal signals, including leptin, dopamine, somatostatin, insulin, and adrenergic signalling, to influence thyroid hormone synthesis[10].

The nocturnal Thyroid Stimulating Hormone (TSH) peak is diminished or absent in DM patients, and the hypothalamic TSH response to TRH is compromised, resulting in hypothyroidism[11].

Thyroid and diabetes are close to each other, and reversible decreases in thyroxine 5'deiodinase activities and liver concentration are due to hyperglycemia[12]. Insulin resistance and higher levels of circulating insulin have a proliferative impact on thyroid tissue, and the production of thyroid hormones, thus causing thyroid dysfunction in diabetic patients[13].

Thyroid dysfunction results in increased thyroid gland size and nodule development in patients with type 2 DM leading to hyper thyroidism[14]. There are several other mechanisms that thyroid hormones influence glucose metabolism and its related mechanisms in diabetic patients[15].

Uncontrolled DM has been linked to low Triio do thyronine (T3) levels.

This has been linked to a problem with peripheral T4 to T3 conversion, which normalizes when glycaemic management improves[16]. Thyroid illness is more common in diabetic patients; particularly those who have poor glycaemic control, and other co-morbid conditions, hence the real fact of thyroid dysfunction in diabetic patients are still unclear[17]. Thyroid abnormalities are quite common in people with type 2 diabetes mellitus, and they are more common in elderly women with uncontrolled diabetes[18].

Jonklaas, J et al., describe that many studies have examined the prevalence of thyroid dysfunction in diabetes patients, but very few have examined the risk factors for thyroid dysfunction in diabetic patients, and the author adds a note that there is a need for these further investigations [19].

Khassawneh, A. H et al., narrates that we need to identify whether thyroid dysfunction is closely related to some of the mechanisms involved especially the duration of diabetes in Type 2 DM patients[20].

Rahman, S. T., et al reported that access to medical diagnosis and factors relating to thyroid cancer are at the highest risk of over-diagnosis of thyroid cancer.

The author adds a note that better and specific diagnostic tools are needed to differentiate between the indolent thyroid cancer and other thyroid dysfunction[21].

Kuo, E. J., et al reported, that active surveillance is important to increase the detection of under-diagnosed thyroid cancer, and active surveillance is important to reduce the unnecessary treatment of the wrong diagnosis of any thyroid dysfunction[22].

With the above all authors' publication, it is very clear, that thyroid dysfunction is under-diagnosed, and un-reported, with no specific diagnostic tool for thyroid dysfunction, closely related diabetes, with several hidden facts of clinical mechanism, hidden unknown associations between glucose metabolism and thyroid dysfunction, and requires active surveillance for proper diagnosis, and reporting of thyroid dysfunction, hence, this present study was conducted as active surveillance to unknot the fact behind the hidden mechanism between the thyroid dysfunction, age of the patients, and duration of diabetes.

Our present study was also conducted for a great burden that the thyroid cancers were under-diagnosed leading several individuals to death.

When diagnosed with the enlarged size of thyroid nodules, the patient ends up in the final stage of his or her life, hence diagnosing thyroid dysfunction at a specific, and correct time of an individual is essential and we do not have diagnostic tools for diagnosing thyroid cancer in the first stage itself, hence this present study was done as active surveillance first identifying the thyroid dysfunction

(when patient reports as small enlargement in the thyroid nodule) in common population, not after the patent reports as diabetic.

Ethical clearance

The study was pre-informed to the Institutional Ethical Committee and received the ethical clearance to conduct the study.

Inclusion criteria

The patients who visited the hospital for thyroid-related clinical issues were selected for the study for a period of 6 months from June 2021 to December 2021.

Exclusion criteria

Infants, women in gestation, and moribund patients were not included in the study.

Materials and methods

Methodology

Study Subjects : 584 patients were observed, analyzed, and results were recorded for thyroid functionality and its related clinical profile. This study is conducted in the diabetic clinic of the Regional Institute of Medical Sciences (RIMS), Imphal from June 2021 to December 2021.

Patient's History and Clinical details

The selected 584 patient's medical profiles were recorded on visits to the hospital; required investigations were done and recorded. Patient details such as geographical area, gender, age, and occupation, as the objective of the study is thyroid dysfunction, the Intake of Iodine is also recorded, thyroid positivity, history of diabetes, and duration of diabetes were recorded.

Sample collection and Analysis

Blood samples were collected for diabetic marker and thyroid marker after a 12-hour overnight fast. The samples were processed in Boisen S-Line Lab for diabetic markers and results were recorded based on American Diabetes Association[23], and Blood glucose levels of 80–180 milligrams per decilitre (mg/dL) were considered diabetic and if the patient's history detects diabetes, the test was reconfirmed by fasting and postprandial blood glucose after 2 hours of the meal. The results and duration of diabetes were recorded.

For thyroid markers, a Microplate ELISA kit (Model no: CA 92627, Monobind Inc., Lake Forest, CA, USA, 2012, kit was used to analyze Anti-thyroid antibodies (TPO Ag and Tg Ab)[24]. The patients having positivity for thyroid were recorded after their blood detects the antibodies to thyroid markers such as Anti-TPO Ab and Anti-Tg Ab. Anti-thyroid antibodies levels of Anti-TPO Ab = (>40 IU/ml) & Anti-Tg Ab = (>100 IU/ml) [25] were considered normal levels based on the assay, patient's thyroid markers levels above the normal levels were considered as elevated levels of thyroid markers and these values were recorded

Quality Assurance

First the quality controls provided in the assay were analyzed which served as standard operating value for both diabetes and thyroid assay to ensure the quality of the assay that performed during this study.

Statistical Analysis

Data were entered in IBM SPSS Statistics software version 20. Means and standard deviation were calculated for continuous data like age, and percentages were calculated for categorical variables, like sex, Tg Ab status, TPO Ab status, etc.

The Chi-square test and Fisher's Exact test were used to compare the predictors like Tg Ag, and TPO Ag with the age of the patients and duration of diabetes. A linear trend line was drawn for the age distribution vs. presence of thyroid markers, and duration of diabetes in both genders with a marking of R^2. Significant at a 5% level with a p-value < 0.05 was considered significant.

Results

A total of 584 patients have been selected for this study. Patient histories and all results of investigations were first analyzed to identify the basic characteristics of the thyroid study population.

Table 1 describes the basic characteristics of the thyroid study population, and 244 (41.4%) patients were hill residents of a geographic area, whereas 340 (58.2%) patients were from a valley geographical area. Males were 198 (33.9%) and females were 386 (66.1%) with a mean age of (Mean ± SD) 46 ± 16.44. The age of the patients was categorized further, and ≤ 29 years were 125 (21.4%), 30-49 years were 180 (30.8%), 50-69 years were 240 (41.1%), and >70 years were 39 (6.7%).

We recorded the occupation of the patients also, and students were 158 (27.1%), Housewives/ Unemployed were 319 (54.6%), Government Employees were 62 (10.7%), and those who were involved in business were 45 (7.7%). As this study is on thyroid dysfunction, recording intake of Iodine was essential and all 584 (100%) patients are taking Iodine (Table 1).

We further analyzed the collected data, and found, thyroid positivity was, out of 584 patients, 315 (53.9%) patients had thyroid positivity. TPO Ab were 103 (32.7%), Tg Ab were 169 (53.7%), and both TPO Ab and Tg Ab were 43 (13.6%). The patients were analyzed for diabetic markers and found diabetics were 200 (34.2%), and non-diabetics were 384 (65.8). the duration of diabetes was recorded, analyzed, and categorized into ≤ 4 years of duration of diabetes were 68 (34.0%), 5-10 years 85 (42. 5%), 11-20 years 40 (20.0%), and >20 years 7 (3.5%) (Table 1).

Table 1: Basic Characteristics of Thyroid Study Population

Variables	No (%)
Geographical Area	
Hill	244 (41.4)
Valley	340 (58.2)
Gender	
Male	198 (33.9)
Females	386 (66.1)
Age Categories (in years) (Mean ± SD) – 46± 16.44	
≤ 29 years	125 (21.4)
30-49 years	180 (30.8)
50-69 years	240 (41.1)
>70 years	39 (6.7)
Occupation	
Students	158 (27.1)
Housewife/Unemployed	319 (54.6)
Government Employees	62 (10.7)
Business	45(7.7)
Intake of Iodine	
Yes	584 (100.0)
No	0 (0.00)
Thyroid Positivity (n=315)	
TPO Ab	103 (32.7)
Tg Ab	169 (53.7)
TPO Ab and Tg Ab	43 (13.6)
History of Diabetes	
Diabetic	200 (34.2)
Non-diabetic	384 (65.8)
Duration of Diabetes (n=200)	
≤ 4 years	68 (34.0)
5-10 years	85 (42.5)
11-20 years	40 (20.0)
>20 years	7 (3.5)

We further analyzed the association of age of non-diabetics and the thyroid markers in both genders in table 2. We have excluded the diabetics in this analysis due to the reason, diabetes may alter the result. Out of 584 patients, 384 were non-diabetic, and among them, 202 patients showed positivity for thyroid markers. Out of 202 patients, among them 37 (18.3%) patients were males, and 165 (81.7%) patients were females.

Among 202 patients who were found positive for thyroid markers, 32 patients showed positivity for TPO Ab, among them, males were 4 (12.5%), and females 28 (87.5%). Among the 202 patients who found thyroid positivity in non-diabetic patients, 142 patients showed positivity for Tg Ab, among them, males 31 (21.8%), and females were 111 (78.2%) with a statistical significance of 0.0469. Among the 202 thyroid markers positive patients, 28 patients showed positivity for both TPO Ab,

and Tg Ab, among them, males were 2 (7.1%), and females were 26 (92.9%) (Table 2).

We additionally analyzed, the association of age by categorizing the age groups in relation to TPO Ab positivity in both genders, and presented in table 2. Among the 202 thyroid markers positive patients in non-diabetic, 32 were found positive for TPO Ab, among them, ≤ 29 years of age groups were 6, among them, males were 3 (50.0%), and females were 3 (50.0%) with statically significance of 0.0021, in the age group of 30-49 years 11 were positive for TPO Ag, males were 1 (9.1%), and females were 10 (90.9%), in 50-69 years of age group 13 were found positive for TPO Ag, no males were found positive in this age category, whereas 13 females found positive with 100.0%, and in the age group of ≥70 years 2 were found positive for TPO Ag, both were females (100.0%) and no males found positive in this age group (Table 2).

Out of 202 thyroid markers positive non-diabetic patients, Tg Ab was positive in 142 patients, among them 31 (21.8%) were males and 111 (78.2%) were females. Among the 142 Tg Ab positive patients, in the ≤ 29 years of age group were 37, among them, males 11 (29.7%), and females were 26 (70.3%), in the 30-49 years age group was 52, males were 7 (13.5%), and females were 45 (86.5%), in the age group of 50-69 years 42 patients were positive for T gab, among them males were 11 (26.2%), and females were 31 (73.8%), in ≥70 years of age group 11 patients were positive for Tg Ab, among them, males were 2 (18.2%), and females were 9 (81.8) (Table 2).

In table 2, we have furnished the association of age of non-diabetics and both TPO Ag. Out of 202 non-diabetic thyroid markers positive patients, 28 patients were positive for both TPO Ag and Tg Ab, among them males were 2 (7.1%), and females were 26 (92.9%).

Among 28 both TPO Ag and Tg Ab positive patients, 5 were in the age group off ≤ 29 years, among them, males were 2 (40.0%), and females were 3 (60.0%) with statistical significance of 0.0265, in 30-49 years age group were 9 (100.0%) patients were found positive for both TPO Ag, and Tg Ab, and all of them were females. In the age group of 50-69 years, 13 patients were positive for both TPO Ag & Tg Ab, and all 13 (100.0%) patients were females. In the age groups of ≥70 years, 1 (100.0%) female patient was found positive for both TPO Ag and Tg Ab (Table 2).

Table 2: Association of age and thyroid makers in both genders in Non-diabetic Patients

Non-Diabetic (n=384)			
Thyroid Hormones (n=202)	Male (n=37) 18.3%	Female (n=165) 81.7%	P-value
TPO Ab (n=32)	n=4 (12.5)	n=28 (87.5)	0.3536
Tg Ab (n=142)	n=31 (21.8)	n=111 (78.2)	0.0469*
TPO Ab and Tg Ab (n=28)	n=2 (7.1)	n=26 (92.9)	0.0996
TPO Ab (n=32)			
Age Groups (n=32)	Male (n=4) 12.5%	Female (n=28) 87.5%	P-value
≤ 29 years (n=6)	n=3 (50.0)	n=3 (50.0)	0.0021*
30-49 years (n=11)	n=1 (9.1)	n=10 (90.9)	0.6730

50-69 years (n=13)	n=0 (0.00)	n=13 (100.0)	0.1277
≥70 years (n=2)	n=0 (0.00)	n=2 (100.0)	0.9998
Tg Ab (n=142)			
Age Groups (n=142)	Male (n=31) 21.8%	Female (n=111) 78.2%	P-value
≤ 29 years(n=37)	n=11 (29.7)	n=26 (70.3)	0.1762
30-49 years(n=52)	n=7 (13.5)	n=45 (86.5)	0.0665
50-69 years(n=42)	n=11 (26.2)	n=31 (73.8)	0.4151
≥70 years(n=11)	n=2 (18.2)	n=9 (81.8)	0.7603
TPO Ab &Tg Ab (n=28)			
Age Groups (n=28)	Male (n=2) 7.1%	Female (n=26) 92.9%	P-value
≤ 29 years(n=5)	n=2 (40.0)	n=3 (60.0)	0.0265*
30-49 years(n=9)	n= 0 (0.00)	n=9 (100.0)	0.5476
50-69 years(n=13)	n= 0 (0.00)	n=13 (100.0)	0.4841
≥70 years(n=1)	n= 0 (0.00)	n=1 (100.0)	0.9996

Chi-square test *-Statistically Significant

Fisher's exact test

We further away, analyzed the association between the duration of diabetes and thyroid markers in both males and females as represented in Table 3. Out of 584 patients, 200 were diabetic, among 200 (34.2%) diabetic patients, 113 were with positivity to thyroid markers. Out of 113 thyroid-positive patients, TPO Ab 71, and among 71 TPO Ab patients, males were 28 (39.4%), females were 43 (60.6%), among 113 thyroid-positive patients, Tg Ab 27, among them, Tg Ab 27, males were 8 (29.6%), and females were 19 (70.4%), and in 15 diabetic patients, both TPO Ab and Tg Ab were positive, among them males were 5 (33.3%), and 10 (66.7%) (Table-3).

We still a step forward, analyzed the association of duration of diabetes and TPO Ag. Among the 71 TPO Ag positive patients, ≤ 5 years were 17, among them males were 5 (29.4%), females were 12 (70.6%), 5-10 years of duration diabetes were 35, among them, males were 12 (34.3%), and females were 23 (65.7%), 11-20 years were 18, among them males were 10 (55.6%), and females were 8 (44.4%), and >20 years 1 patient was male (Table-3).

In table-3, we have explained the association between Tg Ab positivity and duration of diabetes, among the 27 Tg Ab positive patients, ≤ 5 years were 7, among them males were 1 (14.3%), females were 6 (85.7%), 5-10 years of duration of diabetes were 12, among them, males were 3 (25.0%), and females were 9 (75.0%), 11-20 years were 8, among them males were 4 (50.0%), and females were 4 (50.0%), and >20 years were 0 patient.

Among the 15 TPO Ag and Tg Ab positive patients, ≤ 5 years were 1, among them females were 1 (100.0%), and no males were positive, 5-10 years of duration of diabetes were 9, among them, males were 2 (22.2%), and females were 7 (77.8%), 11-20 years were 5, among them males were 3 (60.0%), and females were 2 (40.0%), and in >20 years of duration of diabetes, no patient were positive for both TPO Ag and Tg Ab (Table-3).

Table 3: Association between the duration of diabetes and thyroid makers in both genders in Diabetic Patients

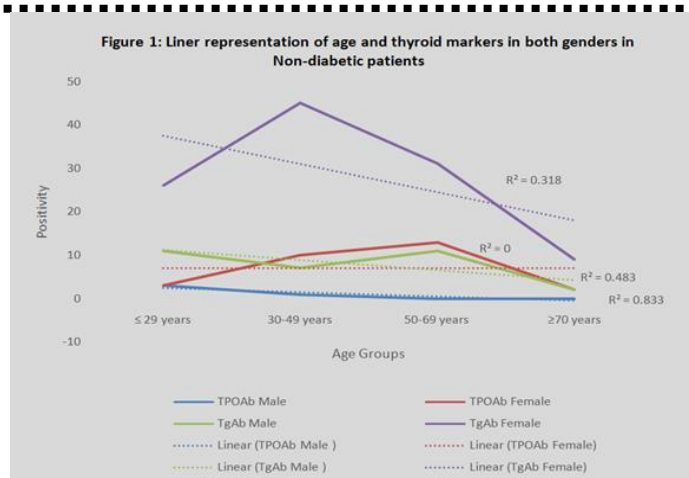
Diabetic (n=200)			
Thyroid Hormones (n=113)	Male (n=41) 36.3%	Female (n=72) 63.7%	P-value
TPO Ab (n=71)	n=28 (39.4)	n=43 (60.6)	0.3647
Tg Ab (n=27)	n=8 (29.6)	n=19 (70.4)	0.4098
TPO Ab and Tg Ab (n=15)	n=5 (33.3)	n=10 (66.7)	0.7986
TPO Ab (n=71)			
Duration of Diabetes (n=71)	Male (n=28) 39.4%	Female (n=43) 60.6%	P-value
≤ 5 years (n=17)	n=5 (29.4)	n=12 (70.6)	0.3321
5-10 years (n=35)	n=12 (34.3)	n=23 (65.7)	0.3812
11-20 years (n=18)	n=10 (55.6)	n=8 (44.4)	0.1053
>20 years (n=1)	n=1 (100.0)	n=0 (0.00)	0.3944
Tg Ab (n=27)			
Duration of Diabetes (n=27)	Male (n=8) 29.6%	Female (n=19) 70.4%	P-value
≤ 5 years (n=7)	n=1 (14.3)	n=6 (85.7)	0.3889
5-10 years (n=12)	n=3 (25.0)	n=9 (75.0)	0.6957
11-20 years (n=8)	n=4 (50.0)	n=4 (50.0)	0.1829
>20 years (n=0)	n=0 (0.00)	n= 0(0.00)	-
TPO Ab &Tg Ab (n=15)			
Duration of Diabetes (n=15)	Male (n=5) 33.3%	Female (n=10) 66.7%	P-value
≤ 5 years (n=1)	n=0 (0.00)	n=1 (100.0)	0.9999
5-10 years (n=9)	n=2 (22.2)	n=7 (77.8)	0.3287
11-20 years (n=5)	n=3 (60.0)	n=2 (40.0)	0.2507
>20 years (n=0)	n=0 (0.00)	n=0 (0.00)	-
>20 years (n=0)	n=0 (0.00)	n=0 (0.00)	-

Chi-square test *****-Statistically Significant

Fisher's exact test

Figure 1 constitutes with the trend line explain the association of age and the thyroid markers positivity in nondiabetic patients. As per figure 1, Tg Ab positivity was found higher in females in the age group of 30-49 years with an R^2 value of 0.318, whereas in males, the Tg Ab was higher in the age group of 50-69 years with an R^2 value of 0.483. In males as age progressed, the TPO Ag positivity decreased, whereas in females TPO Ag positivity was higher in the age group of 50-69 years.

Figure 1: Liner representation of age and thyroid markers in both genders in Non-diabetic patients.



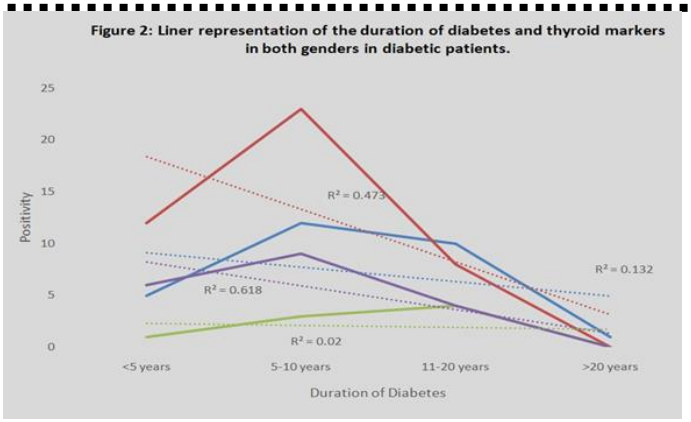


Figure 2 delineates the trend line of the association between the duration of diabetes and thyroid markers positivity in diabetic patients. As the duration of diabetes increased, the positivity of Tg Ab positivity increased in male diabetic patients with an R^2 value of 0.02, whereas in females the positivity Tg Ab was gradually decreased as the duration of diabetes increased, but was found higher in the duration of diabetes 5-10 years with an R^2 value of 0.618.

In females, as the duration of diabetes increased, the positivity of TPO Ab was increased and was found higher in the duration of diabetes 5-10 years, and gradually deceased as the duration of diabetes increased, with an R^2 value of 0.473. In males, as the duration of diabetes increased, the positivity of TPO Ag also increased, and was found higher in the duration of diabetes 5-10 and 11-20 years of duration of diabetes indicating was higher from 5-20 years of duration of diabetes with an R^2 value of 0.132.

Figure 2: Liner representation of the duration of diabetes and thyroid markers in both genders in diabetic patients.

Discussion

Thyroid dysfunction in diabetic patients is a closely related phenomenon, but showing several hidden mechanisms needs to be revealed. Ganie, M. A., et al found in their study conducted in Himalayan valleys tribes, that patients living in the valley are more prone to thyroid dysfunction, and in this study, the author reported thyroid dysfunction in 24.1% who are subclinical identified and 6.8% were showing overt hypothyroidism[26]. In our study, we found that 58.2% of the study population‘s residence was in the valley, and found 53.9% of patients were showing positivity to thyroid markers.

Shi, X., et al reported 24.9% of TPO Ab, and 18.5% of Tg Ab in type 1 diabetic patients, but not provided gender-based information in both genders separately or association of these thyroid markers with any vital factors such as duration of diabetes or gender, whereas out present study reported, TPO Ag as 32.7%, Tg Ab as 53.7%, (0.0469) and both thyroid markers were positive in 13.6% (0.0265) of the patients, we also are reporting the association of thyroid markers with the vital factors such as age-relation in the non-diabetic patient (0.0021), (R^2-0.318), gender-related (R^2-0.483), and the association between duration of diabetes (R^2-0.02) and thyroid markers in diabetic patients[27].

Jonsdottir, B., et al identified in type 1 diabetic individuals, that TPO showed significantly higher positivity than in controls (non-diabetics) than Tg Ab, but our study was presented with high positivity of both TPO Ab, and Tg Ab (0.0469) in non-diabetic also with gender, and age association. Our present study showed that in a ≤29 years of age group, in both genders the positivity of TPO Ab (0.0021) individually was high, and both TPO Ab, and Tg Ab (0.0265) collectively also was high in the ≤29 age group of non-diabetic patients[28].

Positivity rates for TPOA at 41.5%, TGA at 28.3% in published data by Pan, S., et al in type 1 diabetics, whereas our present study reported TPO Ab at 32.7%, Tg Ab at 53.7% individually, both TPO Ab, and Tg Ab in 13.6% of both in diabetic and non-diabetic patients of this present study[29].

Huse bye, E. S., et al reported that Type 1 diabetic patients are at higher risk with co-morbid conditions such as Auto-Immune Thyroid Diseases (AITD), but not reported the gender-based analytical report[30], and our present study reported the positivity of TPO Ag in both type 2 diabetic patients separately, and in non-diabetic patients, indicating, the positivity of TPO Ab is not only higher in diabetic patients, but also in the non-diabetic patient, further leading the under-diagnosed diseases of Auto immune Poly-endo crinopathy Syndrome-II, Hashimoto's thyroiditis and Graves' disease which are more common in residences of valley and hills.

Wang, W., et al describes that autoimmune thyroid diseases especially, Graves' disease and Hashimoto's thyroiditis are the most common co-morbidities of type 1 diabetic patients, and signify by elevation of thyroid markers in type 1 DM patients[31], and our present also accepts this phenomenon by the represented result of high positivity in both type 2 diabetic patients, and even in nondiabetic subjects, indicating that these co-morbidities such as Graves' disease and Hashimoto's thyroiditis are under-diagnosed, and un-reported.

Fisher, S.B., et al reported that follicular thyroid is thyroid cancer, which was diagnosed only during the surgeries, indicating there is no specific differential diagnostic tool for other thyroid dysfunction and thyroid cancer[32].

In conclusion, as the published articles signify that there is a vacuole in the diagnosis of thyroid dysfunction, no specific tool to differentiate between thyroid cancer, and other thyroid dysfunction, and requires active surveillance, our present study reports and recommend that first thyroid dysfunction has to be diagnosed in common population. Further, differentiated thyroid cancer and thyroid dysfunction, several other hidden facts such as thyroid hormones influence glucose metabolism even in non-diabetic patients causing them to an under-diagnosed clinical condition that leads them to mortality with the unknown reason for death. By proper active surveillance, and specific tools we can reduce the mortality of under-diagnosed thyroid dysfunction in patients.

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