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EFFECT OF THYROID ANTIBODIES ON DIABETIC CONTROL IN PEDIATRIC AND ADOLESCENT PATIENTS OF TYPE-1 DIABETES MELLITUS

Hafiz Muhammad Tousif Afzal, Hassan Bin Aziz, Moaz Ahmad
Mayo Hospital Lahore

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Abstract:

Background: *Type-1 DM (Diabetes Mellitus) is an autoimmune disease and this disease has association with many autoimmune abnormalities, availability of the thyroid antibodies could have negatively influenced on the control of diabetes. The aim of this study is to investigate the thyroid autoimmunity in the pediatric and adolescents' patients suffering from Type-1 DM and the effect of the presence of abnormalities of thyroid autoimmunity on the control of diabetes in pediatric patients of Type-1 DM in Pakistan.*

Methodology: *This research work was carried out at Mayo Hospital Lahore. The duration of this study was from January 2019 to July 2020. We analyzed the data of 120 patients suffering from Type-1 DM, having age from 1 to 16 years who got treatment and they were coming for follow-up in our diabetic clinic. Tests of thyroid functions, anti-TG (Antibodies to thyroglobulin) and anti-TPO (Thyroperoxidase) were calculated, recorded and associated with the control of diabetes according to the level of HbA1c (Glycated Hemoglobin).*

Results: *In total 120 patients, positive anti-TG (Antibodies to Thyroglobulin) were higher in ≤ three years group of DM and negative anti-TG was lower in > three years of group of DM with results which were statistically significant (P=0.0430).Concerning the thyroid antibodies (AB) distribution in accordance to the HbA1c group, we found a progressive positive anti-TPO titer with the glycemic status, there was lowest positive anti-TPO for good glycemic control and the group with poor glycemic control had the greatest positive anti-TPO titer and all these findings were significant statistically (P=0.0480).*

Conclusions: *There may be association of the thyroid autoimmunity with poor control of diabetes and elevated level of TSH, showing the sub-clinical hypothyroidism that may have influence on the diabetic control.*

KEYWORDS: *Autoimmunity, Type-1 DM, Glycemic, Hypothyroidism, Hemoglobin.*

Corresponding author:
Hafiz Muhammad Tousif Afzal,
Mayo Hospital Lahore

QR code

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INTRODUCTION:

Type-1 DM as an auto-immune disease, has association with many other auto-immune abnormalities that may have impact on the glycemic control with the disruption of the function of associative organs [1]. The prevalence rate of the positive thyroid antibodies in pediatrics having Type-1 DM varies from 1.0% to 30.0% in different regions of the worlds [2]. Clinical significance of such antibodies is still an issue of full of controversies. Moreover, we found no consensus on auto immune thyroiditis screening in the patients of Type-1 DM [3]. AITD (Auto-Immune Thyroid Disease) is one of the most frequent autoimmune complications associated with Type-1 DM. Its expected incidence is 2 to 4 times higher as compared to the general public [4], most common clinical type is Hashimoto's thyroiditis (12.0% to 26.0%). The Graves' disease is less frequent (0.30% to 5.0%) [5].

The diagnosis and screening of AITD are basedon evaluation of auto-antibodies to anti-TPO and anti-TG.

The rate of prevalence of these auto-antibodies is depending upon the gender, patient's age, and age of the patient at the time of diabetes. There is also variation in these determinants in various regions of world and it is acknowledged as much higher in the regions with higher intake of iodine [6,7]. This research work was carried out to assess the profile of thyroid auto-antibody in patients of Type-1 DM and effect of the presence of abnormalities of thyroid autoimmunity on glycemic control in the patients suffering from Type-1 DM in Pakistan.

METHODOLOGY:

This research work was carried out in Mayo Hospital Lahore. The duration of this study was from January 2019 to July 2020. Total 120 pediatrics and adolescents having age from 1 to 16 years suffering from Type-1 DM who were coming for regular follow-up in our clinic, were the participant s of this research work. We obtained the consent of the guardians of the patient after describing them the purpose of this research work. We collected the detail history of the patients from their parents as patient's name, phone number, age, gender, date of onset of DM and duration of diabetes. We also investigated the past history of any auto-immune disease in the family. We estimated the glycated hemoglobin A. with the use of fast ion exchange Resin Separation Procedure. Results of HbA1c for last one year and averages were calculated and identified as markers for glycemic control as;
HbA1c =6.0-7.90 as good control,
HbA1c=8.0-9.90 as fair control and
HbA1c>10.0 as poor control [8].

Test of thyroid function was calculated as following; 2 ml were obtained and sent for estimation of TSH, T3 and T4. Normal values for T3, T4 and TSH were 1.24 to 2.54 nmol/l, 35.70 to 141.0 nmol/ml, and 0.40 uIU/ml correspondingly. Serum TPO (Anti-thyroid Peroxidase) antibody and anti-TG (Anti-thyroglobulin) antibody was estimated with the use of AESKULISA a-TPO kits, made of Germany. In this current research work, normal range for anti-TPO antibody was lower than 65.0 IU/ml, border line 65 to 113 and positive results were greater than 113.0 IU/ml. For anti-thyroglobulin, normal range antibodies were estimated as normal if antibody titer was lower than 60.0 IU/ml, border line if from 60 to 80 IU/ml and found positive if antibody titer is greater than 80.0 IU/ml. The ethical committee of the institute gave the permission to conduct this research work. We used the SPSS V.23 for the statistical analysis of the collected information. We presented the discrete variables in %. We used the Chi-square test to test the importance of the association for the discrete variable. P-value of less than 0.030 was significant.

RESULTS:

There were total 120 patients in this research work, with response rate of 100.0%. The average age of the patients was 7.52± 2.26 years. Most common age group was present with age from 5 to 10 years constituted 24.0% of the total patients and lowest category of age was <5.0 years constituted 10.0% of the total patients. There were 52% female and 48% male patients. 66% patients were present with the duration of diabetes as less than 3 years. Majority of the patients of this research work were present with negative past family history of auto-immune abnormalities (75.10%). Only 21.0% patients were present with strict glycemic control, whereas 34.50% patients were present with fair glycemic control and 38% patients were present with poor glycemic control. Positivity of thyroid Anti-TPO was 15.10% whereas Anti-TG was positive in only 26.0% patients and 9.58% patients were present with positive results for both tests. There was high concentration of TSH in 10 (4.40%) patients and AITD were newly identified in 2.0% (n: 3) patients.

The patients in age group of >10 years of age had highest positive anti-TPO AB and age group with <5.0 years had lower positive anti-TPO AB but these findings were not much significant. There is variation in the distribution of thyroid AB with the duration of diabetes. Although group of patients with ≤3.0 years

duration had more positive anti-TPO AB titer than the group of patients with >3.0 years, this finding was also not much significant statistically (P=0.150) (Table-1).

Table-I: Distribution of Anti TPO According to Duration Of DM, No. Of Patients 120

Duration of DM AB		Duration of DM				p-value
		≤3 year		> 3 year		
		No.	%	No.	%	
Anti TPO	Positive	12	12%	10	22%	0.15
	Negative	58	84%	40	74%	
Total		70	100%	50	100%	

Positive anti-TG was high in the group of patients with ≤3.0 years duration and negative anti-TG was lower in the group of patients >3.0 years duration. These results were statistically significant(P=0.0430) (Table-2).

Table-II: Distribution of Anti TG According to Duration Of DM, No. Of Patients 120

Duration of DM AB		Duration of DM				p-value
		≤3 year		> 3 year		
		No.	%	No.	%	
Anti TG	Positive	31	31%	7	15%	0.043
	Negative	45	65%	37	81%	
Total		76	100%	44	100%	

About the distribution of the thyroid AB according to group of HbAc1, we found the progressive positive anti-TPO titer with status of glycemic control; there was lowest positive anti-TPO titer for good glycemic control and there was highest positive anti-TPO titer for adverse glycemic control group. These results were significant statistically (P=0.0480), as presented in Table-3.

Table-III: Distribution of Anti TPO According to HBAC1 Group, no. of Patients 120

Thyroid : AB		HBAC1 group						p-value
		Good glycemic control		Fair glycemic control		Poor glycemic control		
		No.	%	No.	%	No.	%	
Anti TPO	Positive	5	10%	4	9%	14	24%	0.048
	Negative	20	86%	41	87%	36	72%	
Total		25	100%	45	100%	50	100%	

Although Anti-TG titer also displays the progressive rise with the poor glycemic status. These findings were not significant statistically (P=0.150) as presented in (Table-4).

Table-IV: Distribution of anti TG According to HBAC1 Group, no. of Patients 120

Thyroid: AB		HBAC1 group						p-value
		Good glycemic control		Fair glycemic control		Poor glycemic control		
		No.	%	No.	%	No.	%	
Anti TG	Positive	6	21%	10	20%	13	34%	0.15
	Negative	19	75%	35	76%	37	62%	
Total		25	100%	45	100%	50	100%	

DISCUSSION:

There were consistent results about the positivity for serum anti-TPO antibodies as reported by current research work with many other studies [9-14]. Low percentage of positive Anti-TPO than anti-TG may be due to the reason that anti-TPO was highly specific than the Anti-TGA [15]. This particular point was also recorded by Berg in his research work and he explained that there was association of Anti-TPO with the high TSH elevation than ATG [16]. There was a strong association between the thyroid auto-antibodies and risk of the thyroid dysfunction in the patients suffering from Type-1 diabetes [17]. Based on auto-antibody's positivity and concentration of TSH, concentration of TSH was much high in 14.0% of studied DM patients and there was positive auto-immunity in all these patients. Whereas overt thyroid dysfunction was present in only 3 females with the presence of hypothyroidism, this finding is consistent with the results of other research works [18, 19].

The calculation of the thyroid functions tests in suspected patients or in the patients with positive TAB (Thyroid Antibodies) would confirm the presence of disease [20, 21]. Thyrotoxicosis may degrade the diabetes control and enhance the requirement for increased dosage of insulin and hypothyroidism can cause the increased incidences of hypoglycemic episodes in the patients of diabetes [22, 23]. Metwalley KA in his research work conducted in Egypt stated that patients of DM with hypothyroidism had much high levels of HbA1c as compared to the patients of DM without hypothyroidism [24].

CONCLUSION:

Screening of auto-antibodies in the patients of Type-1 DM could reveal sub-clinical cases of AITD, but there is limited predictive value for the progression to its clinical manifestations. Patient's follow-up with positive auto-antibodies is much vital because further deterioration of the control of diabetes and malfunction of the associative organ may be the outcome.

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