IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 18, Issue 4 Ser. 8 (April. 2019), PP 10-13
www.iosrjournals.org

Correlation Between Anti Thyroid Antibodies and Diabetic Retinopathy in Type 2 Diabetic Patients

Ahmed A.[1], Waris A.[2], SukulRR[1],RizwiSA.[1], Siddiqi SS.[3]
[1]*MS Ophthalmology, Institute of Ophthalmology, Jnmch, AMU, Aligarh.*
[2]*MS, Fico(UK), Fics(USA), Frcs(Glasg), Frcs(Edin), Institute of Ophthalmology, Jnmch, AMU, Aligarh.*
[3]*MD Medicine, Rajeev Gandhi Centre for Diabetes and Endocrinology, JNMCH, AMU, Aligarh*
Corresponding Author: Dr. Abdul Waris, Institute of Ophthalmology, Jnmch, AMU, Aligarh, India.

Abstract:- ***Objectives:*** *To determine the association between anti thyroid antibodies and diabetic retinopathy in type 2 diabetic patients.* ***Study design:*** *cross sectional (observational) study.* ***Place & Duration of Study:****1The Retina Clinic, Institute of Ophthalmology, Jawaharlal Nehru Medical College, A.M.U., Aligarh and Rajiv Gandhi Centre for Diabetes and Endocrinology, Jawaharlal Nehru Medical College, A.M.U., Aligarh, from January 2017 to February 2018,****Materials & Methods:****Total 60 patients with diabetes mellitus II were enrolled.30 patients with diabetic retinopathy were taken as cases, while a similar number of patients without diabetic retinopathy were taken as controls. Known patients of type 1 diabetes mellitus (T1DM), autoimmune disorders, pregnancy, chronic renal failure and chronic liver disease, Malignancies or history of chemotherapy or radiotherapy within past 1 year were excluded from the study. Anti TPO and Anti TG were measured by* ***Beckman Coulter, Access 2****, which uses the* ***chemiluminescence immunoassaytechnique. Results****: On applying independent t tests to the sample, the p values for Anti TG and Anti TPO in the two groups were 0.499 and 0.280 respectively.* ***Conclusion****: The findings in this study demonstrate that there is no significant difference in the levels of Anti TG and Anti TPO in the two groups (p > 0.05).*

Key words*: Diabetic retinopathy, Anti TG, Anti TPO, Type 2 diabetes mellitus, Autoimmune Thyroid Disorder (AITD)*

Date of Submission: 27-03-2019 Date of acceptance: 11-04-2019

I. Introduction

Autoantibodies to thyroglobulin and thyroid peroxidase are common in the euthyroid population and are weighed secondaryresponses and indicative of thyroid inflammation.

Thyroid Peroxidase

Thyroid peroxidase is a glycosylated membrane-bound enzyme, responsible for oxidation of iodine (I2) and iodination of tyrosyl residues of the Tg molecule[12]. Antibodies react against conformational epitopes which is at the surface of the molecules and against linear epitopes[13]. Polyclonal antibodies from healthy individuals and patients react against the same epitopes. Anti-TPO antibodies from healthy subjects did not block TPO activity or intervene with the blocking activity of anti-TPO antibodies from AITD patients[14], while anti-TPO antibodies from AITD patients can activate complement cascade, damage thyrocytes, and act as competitive inhibitors of enzymatic activity[15]. These antibodies can be of any class of IgG, although some studies indicate a higher prevalence of IgG1 (70%) and IgG4 (66.1%) compared to IgG2 (35.1%) and IgG3 (19.6%)[16]. Low levels of IgA antibodies have also been reported[17]. Anti-TPO antibodies are more common than anti-TG antibodies and suggestive for thyroid disease[17]. Anti-TPO antibodies are inductors of oxidative stress proved by decreased antioxidant potential, advanced glycosylation products and oxygen metabolites in blood[18]

Thyroglobulin

Tyroglobulin is a large (600 kDa) glycoprotein comprising of dimers and containing on average 2–3 molecules of T4 and 0.3 molecules T3. The molecule is heterogeneous concerning hormone content, glycosylation, and size. The production of antibodies against Tg can be produced by massive decimation of the thyroid gland, but high Tg levels in blood do not *per se* cause antibody production. Out of the 40 epitopes that have been linked, according to some authors and 1–2 according to others are immunogenic[19],[20].
Thyroid autoantibodies are not only frequently detected in patients with AITD but also in subjects without obvious thyroid dysfunction. The high prevalence arouses kick regarding a potential role in extra-thyroidal diseases.Clinically,thyroid dysfunction can cause metabolic disturbancesand may subvert diabetes control.

II. Materials And Methods

This cross-sectional study was conducted after taking ethical clearance from Institutional Ethical Committee, Jawaharlal Nehru Medical College and Hospital, A.M.U, Aligarh. Tenets of the Declaration of Helsinki were followed. An informed written consent was taken from each patient and\or patient attendant before participation in the study. The study population was drawn from the diabetic patients who attended the Rajiv Gandhi Center for Diabetes and Endocrinology, and subsequently were referred to the Retina Clinic, Institute of Ophthalmology, of the same hospital, for their ocular evaluation.

A clinical history was taken with the help of a structured questionnaire on a specially designed Performa(Appendix) including- demographic data, duration of diabetes, treatment taken, presence of any other complications of diabetes, addictions, dietary habits, family history of diabetes, and blood pressure.

The laboratory profile of each patient comprised of Blood sugar (both fasting greater than or equal to 126mg/dl in diabetes), HbA1C (greater than or equal to 6.5 % in diabetes),thyroid antibodies (thyroglobulin antibody titerTgAb – expected value below 30 IU/ml , thyroid peroxidase antibody TPO - expected value below 12 IU/ml). The Thyroid profile and Thyroid antibodies was assessed **by Beckman Coulter, Access 2**, which uses the **chemiluminescence immunoassaytechnique.**[10,11]

Total 60 patients with diabetes mellitus II were enrolled.30 patients with diabetic retinopathy were taken as cases, while a similar number of patients without diabetic retinopathy were taken as controls. Known patients of type 1 diabetes mellitus (T1DM), autoimmune disorders, pregnancy, chronic renal failure and chronic liver disease, major depressive disorder, medications affecting thyroid hormones, Malignancies or history of chemotherapy or radiotherapy within past 1 year were excluded from the study.

A diagnosis of diabetic retinopathy was made when a patient exhibited a minimum of one microaneurysm in any field , as well as hemorrhages (dot, blot or flame shaped) and maculopathy (with or without clinically significant macular edema). The diagnosis of proliferative diabetic retinopathy was made only if there is neovascularization. The ETDRS classification was used to categorise the patients into various grades of diabetic retinopathy[12].

SPSS version 20 was used for analysis. Continuous variables were expressed as means, standard deviation (SD) and range. Independent and, paired t test were used as per the type of data. Non parametric, discrete data were evaluated using Chi square. Odds ratio was used to quantify the strength of association. Levene's test was used to assess the equality of variances for a variable calculated across the two groups. The difference was considered significant at a p value of <0.05.

Variable	Control (n= 30)	Cases (n= 30)	p- value
Age (years)	53.89	53.36	p>0.05
HbA1c (%)	7.39±1.16	8.215±1.81	p<0.05
Tg Ab titre(IU/ml)	15.01±22.6	12.09±6.67	p>0.05
TPO Ab titre (IU/ml)	8.41±5.75	12.21±18.19	p>0.05

III. Results

60 type 2 diabetic subjects fulfilling the inclusion criteria were selected from the individuals reporting at Rajeev Gandhi Centre of Endocrinology and Institute of Ophthalmology, Aligarh Muslim University, Aligarh and categorized into group A (cases) and group B (controls).

The clinical characteristics and biochemical data of the study participants are summarized in table I.

Out of the 30 cases in group A (cases), 18 (60%) were female and 12(40%) were male. Among 30 individuals in group B (controls), 16 (53%) were female and 14 (46%) were male (Table-1). Mean age was 53.36 ± 7.69 years in cases and 53.89 ± 7.93 in controls. Descriptive statistics (Mean ± SD) for quantitative variables like age, HbA1c, Anti TPO, Anti Tg antibodies were calculated for both groups as shown in table I. It revealed that in both Group A (cases) and group B (controls), there was no significant difference in the values of Anti TPO and Anti Tg antibodies.

IV. Discussion

In this study, the anti thyroid antibodies were evaluated in the two groups with diabetes mellitus type 2. To the best of my knowledge, this association has not yet been evaluated in India.

The high incidence of autoimmune thyroid disease in T1DM has been reported in many studies before **(Dosi RV and Tandon N, 2010)**[13]. However, thyroid dysfunction in T2DM with DR is a less delved field. Unrecognized thyroid dysfunction may descend metabolic control and clog the management of diabetes.

Altered thyroid hormones have been described in patients with diabetes, especially those with poor glycemic control. In diabetic patients, the nocturnal TSH peak is effaced, and the TSH response to thyrotropin-releasing hormone is impaired. This may be because of possible alteration of posttranslational glycosylation of thyrotropin-releasing hormone, thus impacting its biological activity **(Gürsoy Net al., 1999)**[14].

The prevalence of 26%–61% of autoantibody positivity in T1DM subjects has been reported from North India, with very few dual positive subjects[15-17]. Low antibody seropositivity is a marked feature of T1DM in Asia, majorly in India, compared to Western T1DM population[17-19].

Different studies previously by **Radaideh et al**[20] and **Gonzalez et al**[21] have demonstrated the frequency of TPO-Ab positivity in male and female between patients suffering from type 2 D.M. and non diabetic patients to be comparable.

The discovery in this study demonstrate that there is no significant difference in the levels of Anti TG and Anti TPO in the two groups ($p > 0.05$). On applying independent t tests to the sample, the p values for Anti TG and Anti TPO in the two groups were 0.499 and 0.280 respectively.

V. Conclusion

- One should have a high index of glimmer regarding the presence of thyroid dysfunction among type 2 diabetic patients.
- Results of the present study indicate that frequency of anti thyroid antibodies is not significantly higher in T2DM with retinopathy than in T2DM without retinopathy. ($p > 0.05$)
- The presence of anti thyroid antibody was not a major risk factor for the appearance of diagnosed thyroid dysfunction among the two groups.
- We concede that the current findings are cross-sectional in nature and the availability of prospective data would further improve the confidence in these associations.
- Addendum, optimized control of systemic considerations, which affect the onset and/or progression of DR through intensive, multi disciplinary, holistic approach, can markedly reduce the impairment of vision due to DR.

References

[1]. McLACHLAN SM, Rapoport B. The Molecular Biology of Thyroid Peroxidase: Cloning, Expression and Role as Autoantigen in Autoimmune Thyroid Disease. 1992;13(2):15.

[2]. Le Fourn V, Ferrand M, Franc J-L. Endoproteolytic Cleavage of Human Thyroperoxidase: ROLE OF THE PROPEPTIDE IN THE PROTEIN FOLDING PROCESS. J Biol Chem. 2005 Feb 11;280(6):4568–77.

[3]. Kohno Y, Yamaguchi F, Saito K, Niimi H, Nishikawa T, Hosoya T. Anti-thyroid peroxidase antibodies in sera from healthy subjects and from patients with chronic thyroiditis: differences in the ability to inhibit thyroid peroxidase activities. ClinExpImmunol. 2008 Jun 28;85(3):459–63.

[4]. Kaczur V, Vereb G. Effect of anti-thyroid peroxidase (TPO) antibodies on TPO activity measured by chemiluminescence assay. Clin Chem. 1997;(8):5.

[5]. Xie L-D, Gao Y, Li M-R, Lu G-Z, Guo X-H. Distribution of immunoglobulin G subclasses of anti-thyroid peroxidase antibody in sera from patients with Hashimoto's thyroiditis with different thyroid functional status. ClinExpImmunol. 2008 Nov;154(2):172–6.

[6]. Balucan FS, Morshed SA, Davies TF. Thyroid Autoantibodies in Pregnancy: Their Role, Regulation and Clinical Relevance. J Thyroid Res. 2013;2013:1–15.

[7]. Ruggeri RM, Vicchio TM, Cristani M, Certo R, Caccamo D, Alibrandi A, et al. Oxidative Stress and Advanced Glycation End Products in Hashimoto's Thyroiditis. Thyroid. 2016 Apr;26(4):504–11.

[8]. Latrofa F, Ricci D, Grasso L, Vitti P, Masserini L, Basolo F, et al. Characterization of Thyroglobulin Epitopes in Patients with Autoimmune and Non-Autoimmune Thyroid Diseases UsingRecombinant Human Monoclonal Thyroglobulin Autoantibodies. J ClinEndocrinolMetab. 2008 Feb;93(2):591–6.

[9]. Autoimmune Diseases in Endocrinology, Chapter: Environmental Factors in Autoimmune Endocrinopathies, Publisher: HUMANA PRESS, Editors: Anthony P. Weetman, pp.75.

[10]. C. Ronda, Luminescence From Theory to Applications (Wiley-VCH, New York, 2008).

[11]. Fereja TH, Hymete A, Gunasekaran T. A Recent Review on Chemiluminescence Reaction, Principle and Application on Pharmaceutical Analysis. ISRN Spectrosc. 2013;2013:1–12..

[12]. Grading Diabetic Retinopathy from Stereoscopic Color Fundus Photographs—An Extension of the Modified Airlie House Classification. Ophthalmology. 1991 May;98(5):786–806.

[13]. Dosi RV, Tandon N. A study on prevalence of thyroid auto-immunity in type 1 diabetes mellitus. J Indian Med Assoc. 2010 Jun;108(6):349–50, 355–6.

[14]. Gürsoy N, Tuncel E, Ertürk E, Ar A. The Relationship Between The Glycemic Control and The Hypothalamus-Pituitary-Thyroid Axis in Diabetic Patients. :6.

[15]. Das AK, Shtauvere-Brameus A, Sanjeevi CB. GAD65 and ICA512 Antibodies in Undernourished and Normally Nourished South Indian Patients with Diabetes. Ann N Y Acad Sci. 2006 Jan 24;958(1):247–50.

[16]. Singh AK, Bhatia E, Dabadghao P, Bhatia V, Gellert SA, Colman PG. Role of islet autoimmunity in the aetiology of different clinical subtypes of diabetes mellitus in young north Indians. Diabet Med. 2000 Apr;17(4):275–80.

[17]. Tandon N, Shtauvere-Brameus A, Hagopian WA, Sanjeevi CB. Prevalence of ICA-12 and Other Autoantibodies in North Indian Patients with Early-Onset Diabetes. Ann N Y Acad Sci. 2006 Jan 24;958(1):2147.

[18]. Wenzlau JM, Juhl K, Yu L, Moua O, Sarkar SA, Gottlieb P, et al. The cation efflux transporter ZnT8 (Slc30A8) is a major autoantigen in human type 1 diabetes. ProcNatlAcad Sci. 2007 Oct 23;104(43):17040–5.

[19]. Lan MS, Wasserfall C, Maclaren NK, Notkins AL. IA-2, a transmembrane protein of the protein tyrosine phosphatase family, is a major autoantigen in insulin-dependent diabetes mellitus. ProcNatlAcad Sci. 1996 Jun 25;93(13):6367–70.

[20]. Radaideh AR, Mo MK, Amari FL, Bateiha AE, El-Khateeb MP, Naser PA, Ajlouni BK. diabetes mellitus in Jordan. Saudi Med J. 2004;25(8):1046-50.
[21]. Ortega-González, MD C, Liao-Lo, MD A, Ramírez-Peredo, MD J, Cariño, Biol N, Lira, MD J, Parra, MD A. THYROID PEROXIDASE ANTIBODIES IN MEXICAN-BORN HEALTHY PREGNANT WOMEN, IN WOMEN WITH TYPE 2 OR GESTATIONAL DIABETES MELLITUS, AND IN THEIR OFFSPRING. EndocrPract. 2000 May;6(3):244–8

Dr. Abdul Waris. "Correlation Between Anti Thyroid Antibodies and Diabetic Retinopathy in Type 2 Diabetic Patients." IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 18, no. 4, 2019, pp 10-13.