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The Relation Between Age Related Macular Degeneration and Thyroid Disorders

Mona Abdelkader[1, *], Naglaa Abass[2]

[1]Ophthalmology Department, Faculty of Medicine, Mansoura, Egypt

[2]Medicine Department, Faculty of Medicine, Mansoura, Egypt

Email address:
monaabdelkader78@yahoo.com (M. Abdelkader), naglaaabass@yahoo.com (N. Abass)

[*]Corresponding author

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Abstract: The Purpose of the study was to evaluate the association between thyroid -stimulating hormone (TSH), free tri-iodothyronine (T3), free thyroxine (T4), hypothyroidism, hyperthyroidism and age related macular degeneration (ARMD) incidence. Nine hundred and fifty patients with thyroid disorders versus five hundred and thirty eu-thyroid subjects were included in the study during the period from January 2014 to February 2019. Blood pressure, blood sugar level and cholesterol, smoking state were estimated. TSH, T3&T4 were measured. Retinal photography and optical coherence tomography were performed. Patients with hyperthyroidism had increased incidence of ARMD. Patients using thyroxine had also increased incidence of ARMD than non using of thyroxine. There were statistically higher significant percent of marriage, educational level and smoking in patients with thyroid disorders with ARMD than euthyroid (p=0.03. 0.06, 0.001 respectively). In thyroid disorders patients, there were a significant differences between patients had ARMD or had not as regard diabetes, hypertension and cholesterol level (p=0.04, 0.09, 0.03 respectively). We concluded that there were increased incidence of ARMD in both hyperthyroidism, and patients use the thyroxine.

Keywords: TSH, T4, T3, ARMD

1. Introduction

Age related macular degeneration (ARMD) is important cause of visual loss [1, 2].

The pathophysiology of ARMD is complex. Drusen is initiated by inflammatory cells and activated by complement formation while the cause of pigment alteration is still unclear. Thyroid hormones regulate different visual functions. Human retinal pigment epithelial (RPE) cells express thyroid hormone receptors that is target for thyroid hormone [3].

Suppression of thyroid hormone preserves cone photoreceptors in mouse with retinal degeneration while, administration of active thyroid hormone deteriorates cones. [4].

Thyroid dysfunction prevalence incidence is 10%. [5, 6].

Alteration of lipid levels, atherosclerosis, and hypertension are predisposing factors for ARMD development which also present in thyroid diseases. [7].

The use of thyroid hormones is associated with ARMD. [8, 9], but this relation did not confirm that. [10].

So, we do this study to detect the relation between thyroid disorders and thyroid hormones and ARMD.

2. Patients and Methods

This study was carried out on patients attending the Outpatient Clinic of Mansoura Medicine Hospital from January 2014 to February 2019.

The study was approved by the Local Ethical Committee of Mansoura University and all patients signed a written informed consent before participating in the study.

A total one thousand and four hundred and eighty patients (two thousand and nine hundred and sixty eyes) were included in the study. Nine hundred and fifty had thyroid

disorders, of whom, five hundred and twenty (520) had hyperthyroidism and four hundred and thirty (430) had hypothyroidism. Five hundred and thirty were euthyroid.

All patients included in this study underwent fundus photography Topcon corporation, 2000, TRC, 5011, japan) and optical coherence tomography (OCT) after mydriasis with mydriacil eye drop.

Two 35° photographs of the macula of both eyes were taken.

ARMD charterized by presence of one of the following drusen, RPE atrophy, choroidal neovascularization, retinal pigment epithelium detachment and neurosensory detachment.

2.1. Exclusion Criteria

Patients with corneal abnormalities, glaucoma, ocular trauma, retinal detachment, any other retinal pathology, ocular inflammation or infection, and psychiatric diseases

2.2. Optical Coherence Tomography

Were performed using spectral domain OCT [Topcon 3D-OCT 1000 Mark II, Tokyo, Japan, software version 3.20].

2.3. Assessment of Thyroid Dysfunction

TSH, T3, T4 were measured.

Hypothyroidism was detected as increased TSH in the presence of either normal or abnormal serum T4, T3. While hyperthyroidism was determined by low TSH in the presence of either normal or abnormal serum T4, T3.

2.4. Assessment of Variables

Systolic and diastolic blood pressure was measured twice using mercury sphygmomanometers. Hypertension was defined as a systolic blood pressure $\geq$ 140 mmHg or a diastolic blood pressure $\geq$ 90 mmHg. Blood sugar and Cholesterol were measured. Smoking state (whether never smoked, past smoker, current smoker), frequency of consuming fish were reported. Education level, marital status life style (walking, exercises) were reported and analyzed.

2.5. Statistical Analyses

Statistical analysis were analyzed by SPSS program versions 17 using Microsoft Windows 7 (SPSS Inc., Chicago, IL, USA). Spearman correlation coefficient is used for correlation between variables. If P = 0.05, considered statistical significant.

3. Results

3.1. Number of the Study

The study included 950 patients with thyroid disorder and 530 euthyroid subjects. The mean age of patients with thyroid disorder was 63.6 ± 5.1 years (range 50-72), while the mean age of euthyroid subjects was 65.8 ± 5.2 years (range 52-78). There was no statistically significant difference between patients with thyroid disorders and euthyroid subjects regarding age, gender, smoking, walking, exercise, presence of hypertension, diabetes mellitus. Walking, exercise, fish consumption).

3.2. Demographic Features

Demographic features were included in tables 1 and 2.

Table 1. *Demographic features of thyroid disorders patients (N=950).*

features	No incident ARMD	Incident ARMD	*P* - value**
Number	**N =695**	**N = 255**	
Age, years	62.6 (4.6)	62.9 (5.1)	0.9
Sex, Female Number Percentage %	390 (56%)	150 (58%)	0.4
Diabetes Number Percent%	91 13%	55 21.5%	0.04
Cholesterol, mmol/L	6.1 (1.2)	6.5 (1.1)	0.3
Smoking, (current) Number Percent%	200 28,7%	100 39,2%	0.05
Hypertension, Number Percent%	260 37,4%	113 44,3%	0.09

This table shows high incidence of ARMD in diabetic, hypertensive smoking, thyroid dysfunction patients.

Table 2. *Demographic features of euthyroid subjects (530 in number).*

features	No incident ARMD	Incident AMD	*P* – value
Number	**N=450**	**N = 80**	
Age, years	60.5 (4.6)	61.9 (4.1)	0.9
Sex, Female Number Percentage %	250 (5.65%)	50 (6.2%)	0.4
Diabetes Number Percent%	85 18,8%	35 .43,7%	0.04
Cholesterol, mmol/L	6.1 (1.2)	6.5 (1.1)	0.03
Smoking, (current) Number Percent%	50 11.1%	55 68,7%	0.05
Hypertension, Number Percent%	210 46,6%	63 78,7%	0.03

This table shows high incidence of ARMD in diabetic, hypertensive smoking euthyroid patients.

3.3. The Relation Between Thyroid Disorders and Marriage

There were statistically higher significant percent of marriage, educational level and smoking in patients with thyroid disorders with ARMD than euthyroid (p=0.03. 0.06, 0.001 respectively).

In thyroid disorders patients, there were a significant differences between patients had ARMD or had not as regard diabetes, hypertension and cholesterol level (p=0.04, 0.09,

0.03 respectively).

3.4. The Relation Between ARMD Incidence and Thyroid Hormons

There were increase incidence of ARMD with abnormal TSH, T3, T4 (Table 3, Figures 1-3).

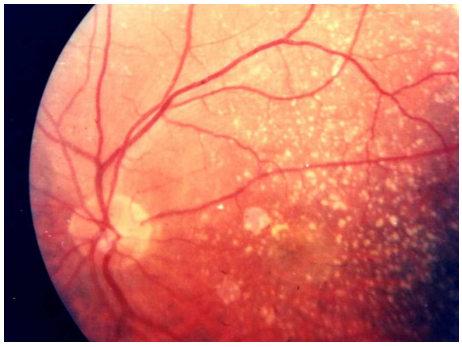


Figure 1. *Patient with hypothyroidism on thyroxine treatment had drusen.*

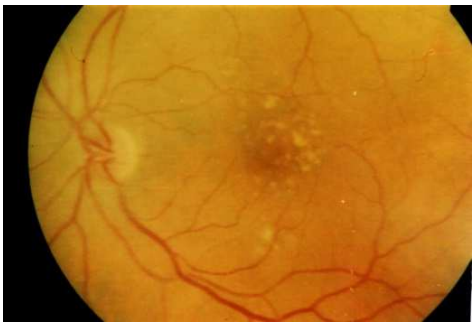
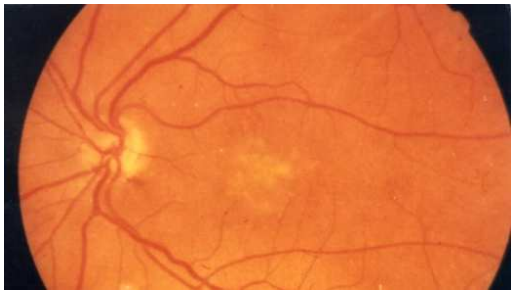
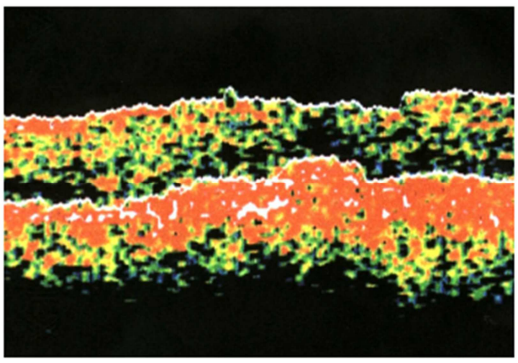


Figure 2. *Patient with hyperthyroidism had large drusen.*



a)



b)

Figure 3. *a) Patient with hypothyroidism had retinal pigment epithelium atrophy; b) OCT of patient withy retinal pigment epithelium atrophy.*

3.5. The Correlation Between Thyroid Hormons and ARMD

There were weak correlation between abnormal TSH and ARMD. There were strong correlation between T3 & T4 and ARMD (Table 4).

There were strong correlation between patients using thyroxine and ARMD incidence than non user in hypothyroidism (table 5).

Table 3. *Association between TSH, T3, T4, and risk of AMD in patients with thyroid disorders.*

Hormones	Incident AMD	no AMD	Total number
High TSH, mIU/L			
With thyroxine	64, (14,8%)	151 (35,1%)	430
Without thyroxine treatment	12, (2.7%)	203, (47.2%)	
Low TSH	95,	425	520
Number %	18.2%	81.7%	
High T3	102	418	520
Number %	19,6%	80.3%	
Low T3			
With thyroxine	105 (24.4%)	103 (23.9%)	430
Without thyroxine treatment	25 (5.8%)	197 (45.8%)	
High T4	209	311	
Number %	40.1%	59.8%	520
Low T4			
With thyroxine	113 (26.2%)	90 (20.9%)	430
Without thyroxine treatment	26 (6%)	201 (46.7%)	

This table shows high incidence of ARMD in hypothyroidism patients using thyroxine.

It shows high incidence of ARMD in patients with abnormal thyroid hormones.

Table 4. *Correlation between thyroid hormones and ARMD incidence.*

Thyroid hormones	ARMD	P
	R	
High TSH	0.3	0.9
Low TSH	-0.33	0.45
High T3	0.5	0.02
Low T3	-0.56	0.04
High T4	0.63	0.001
Low T4	-0.66	0.007

This table shows:

Insignificant weak correlation between TSH & ARMD.

A significant strong correlation between T3, T4 & ARMD.

Table 5. *Correlation between thyroxine treatment & ARMD incidence.*

Thyroxine treatment	ARMD	P
	R	
Using thyroxine	0.71	0
Non using	0.1	0.98

This table shows: strong significant correlation between thyroxine use and ARMD.

3.6. The Percentage of ARMD in Eu Thyroid and Thyroid Disorders

In thyroid dysfunction patients, there were 195 (20.5%) patients had drusen, 49 (5.1%) patients had RPE atrophy, 11 (1.2%) patients had choroidal neovascularization (CNVs).

In eu-thyroid subjects there were 63 (11.9%) patients had drusen, twelve patients (2.3%) had RPE atrophy, five patient (0.94%) had CNVs.

4. Discussion

In this study, the relation between thyroid diseases and ARMD incidence was evaluated since thyroid is risk factor for ARMD and there were few studies about ARMD and thyroid and the results of these studies are inconstant. Some studies said that thyroid hormones use is associated with AMD [11, 12] while others did not comfirm that. [10]

In this study, An abnormal T3, T4, were associated with an increased incidence of AMD while the abnormal TSH is not associated with such increase. Also, the use of thyroxine is associated an increased in ARMD.

Bromfield *et al*. observed an increased ARMD in hypothyroidism as the risk factors for both are the same. [11]

Also, Anand *et al*. found a relation between thyroid hormone use and geographic atrophy. [9]

Similarly, the Beaver Dam Eye study observed an association between thyroid hormone and ARMD [12].

Rotterdam Study said that higher T4 were associated with increased ARMD, [13]. Chatziralli, et al found association between thyroidopathy and ARMD [14], and Ding, et al said that retinal suppression of thyroid hormone signaling, represents a new method for RPE protection and ARMD management. [15] While Gopinath et al did not confirm the significant positive association between T4 and ARMD. [16]

There are different causes for the association between thyroid hormones and ARMD.

First, In a mouse, suppression of thyroid hormone resulted in preservation of cone photoreceptors While stimulating thyroid hormone signaling deteriorates cone. [17, 18]

Second, Nguyen-Legros suggested that thyroid hormone led to a higher photoreceptors turnover and retinal degeneration. Increase of photoreceptors turnover by thyroid hormone change RPE cells distress resulting in macular pigmentary changes. [19]

Third, Hypertension, cholesterol, diabetes, act as mediators through which thyroid function is related to ARMD. [20]

Fourth, oxidative damage to the RPE is the core lesion of ARMD, this is a pathway through which hyperthyroidism cause ARMD. [21, 22]

5. Conclusion

There were an increase in ARMD incidence in patients with abnormal T4, T3 and in patients using thyroxine. Every patient with thyroid disorders must do fundus examination every year at least for early discovery of ARMD to avoid occurrence of wet type of ARMD and blindness (as a complication of wet ARMD).

Conflicts of Interest

There are no conflicts of interest to declare.

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