VITAMIN D LEVELS IN GRAVES' DISEASE WITH AND WITHOUT EXOPHTHALMOS : A CASE-CONTROL STUDY

Sheriba N[1], Abu Shady MM[1], Abdelsalam MM[1] and Eliwa TF[2]

[1]Internal Medicine and Endocrinology Department, [2]Ophthalmology Department, Faculty of Medicine, Ain-Shams University, Cairo, Egypt

INTRODUCTION

Current studies have related vitamin D deficiency with several autoimmune disorders e.g. type 1 DM. In view of those associations, it has been suggested that vitamin D is an extrinsic factor capable of affecting the prevalence of autoimmune diseases.

Graves' disease is an autoimmune disease. Graves' ophthalmopathy is the most common extrathyroid manifestation of Graves' disease and affects 25% to 50% of patients with Graves'disease. Approximately 28% of patients with Graves' ophthalmopathy present as severe cases, with restricted mobility, diplopia, keratopathy, and optic neuropathy.

AIM OF STUDY

The aim of work is to study if there is any difference between vitamin D levels in subjects having Graves' disease with and without exophthalmos.

SUBJECTS AND METHODS

Eighty five (85) adult Egyptian individuals aged between 20-40 years participated in our study. The participants were divided to 3 groups as follows: Group 1: included 30 patients with Graves' disease with exophthalmos. Group 2: included 30 patients with Graves' disease without exophthalmos. Group 3: included 25 healthy volunteers.

Exclusion criteria:

1. Patient taking vitamin D supplementation or any drugs affecting vitamin D level.
2. Patients with chronic kidney disease (CKD).
3. Patients with DM.
4. Patients with other causes of exophthalmos.

All participants were subjected to the following:

1. Full history taking emphasizing on sun exposure, dietary habits and Graves' disease treatment duration and dose.
2. Clinical examination.
3. Full ophthalmological examination to assess eye signs and Hertl's exophthalmometer to assess the degree of exophthalmos.
4. Thyroid profile (FT3, FT4, TSH).
5. Measurement of 25(OH) vitamin D level in blood by ELISA.
6. Thyroid ultrasound. Graves disease was diagnosed by clinical and biochemical symptoms of hyperthyroidism, goiter and eye signs.

RESULTS

Table (1): Description of all data in the 3 studied groups (Grave's with exophthalmos, Grave's without exophthalmos & controls):

	Group 1 mean±SD	Group 2 mean±SD	Control mean±SD
Age (Yrs)	29.8 ± 5.55	29.1± 6.14	27.6± 4.9
M/F	14/16	15/15	13/12
Disease duration (ms)	9.93±3.87	4.83±2.81	
Carbimazole dose (mg/day)	17.33±5.97	9.00±4.23	
Carbimazole duration (ms)	9.46±3.69	4.76±2.78	
Rt. Exophthalmometer (mm)	20.6±1.35	16.9±0.54	16.9±0.67
Lt. exophthalmometer (mm)	20.7±1.11	16.8±0.68	16.9±0.67
V.D status ng/ml	7.82±2.63	20.1±11.9	19.3±11.2

Table (2): Comparison between the 3 studied groups as regard their exopthalmometer examination using ANOVA test

Exopthalmo-meter examination	Group 1 (n=30)	Group 2 (n=30)	Controls (n=25)	ANOVA	P-Value	Post-Hoc test
Exopthalmo-meter (Rt) mm #	20.6 ± 1.35	16.9 ±.54	16.9 ±.67	147.373	0.000**	(1,2), (1,3)
Exopthalmo-meter (Lt) mm#	20.7 ± 1.11	16.8 ± 0.68	16.9 ± 0.67	188.427	0.000**	(1,2), (1,3)

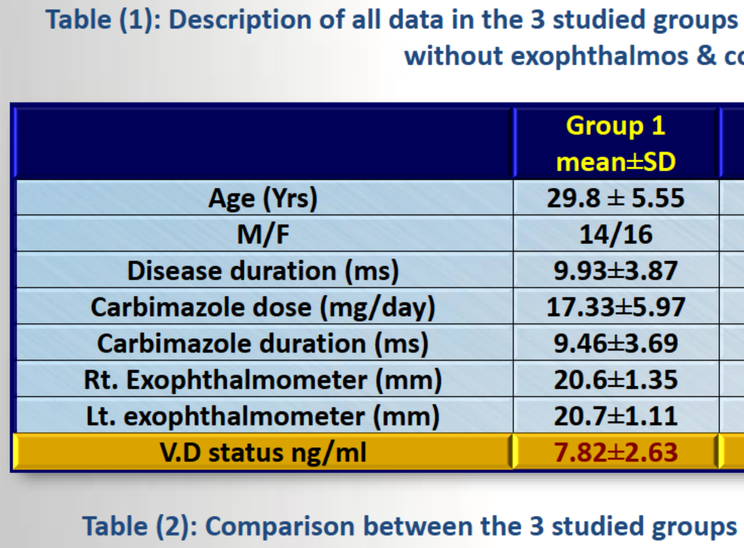


Figure (1): Comparison between the 3 studied groups as regard TSH measurement

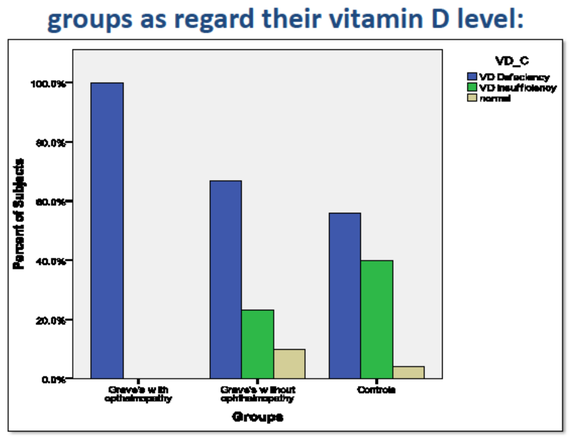
Table (3): Comparison between the 3 studied groups as regard their Vitamin D status using ANOVA test and post-Hoc test

Vitamin D	Group 1 (n=30)		Group 2 (n=30)		Controls (n=25)		ANOVA	P-Value	Post-Hoc test #
Vitamin D(ng/ml)	7.82 ± 2.63		20.1 ± 11.9		19.3 ± 11.2		15.523	0.000**	(1,2), (1,3)
Vitamin D Levels	No	%	No	%	No	%	x2	P-value	
Deficiency	30	100.0	20	66.7	14	56.0	18.356	0.001**	
Insufficiency	0	0.0	7	23.3	10	40.0			
Normal	0	0.0	3	10.0	1	4.0			

(**) significant at P<0.01 by ANOVA test# (1,2)=Significant difference between (Grave's with exophthalmos), (Grave's without exophthalmos) by post Hoc test. (1,3)=Significant difference between (Grave's with exophthalmos) and (controls) by post Hoc test.

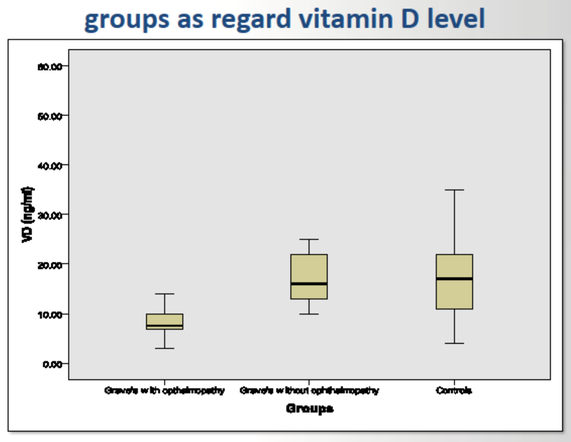
It shows that there is a difference between 3 studied groups as regard vitamin D Levels (P<0.01) using ANOVA test. #; Post Hoc test reveals that there is a difference within groups (1, 2), (1, 3). All subjects in group 1 were vitamin D deficient (100%). In group 2, 66.7% were vitamin D deficient, 23.3% were insufficient and 10% were normal. In the control group 56% were vitamin D deficient, 40% were insufficient and 4% were normal.

Figure (2): Comparison between the 3 studied groups as regard their vitamin D level:



It shows that there is a significant difference between 3 studied groups as regard vitamin D level (P<0.05).

Figure (3): Comparison between the 3 studied groups as regard vitamin D level



It shows that there is a significant difference between 3 studied groups as regard vitamin D level (P<0.05).

Table (4): Correlation between Vitamin D Level and all Studied Parameters in Graves' disease patients with exophthalmos (Group 1) using Pearson correlation

Variables	Vitamin D	
	Pearson Correlation	Sig. (2-tailed)
Age (years)	.049	.797
Disease Duration (ms)	-.106	.577
Carbimazole Dose (mg/d)	-.150	.465
Carbimazole Duration (ms)	-.141	.456
Exopthalmometer (Rt) (mm)	-.394	.031*
Exopthalmometer (Lt) (mm)	-.472	.009**
TSH (MU/l)	.199	0.292
Free T3 (ng/dl)	-.186	0.325
Free T4 (ng/dl)	-.234	0.214

It shows that there is a significant inverse correlation between Serum vitamin D level and exopthalmometer (Lt), exopthalmometer (Rt) measures.

Table (5): Independent predictors of vitamin D levels in the studied subjects (n=85).

Variables	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta		
Constant	49.216	15.679		3.139	.003
Disease Duration (ms)	-.006	.352	-.003	-.018	.986
Carbimazole dose (mg/d)	.281	.209	.176	1.348	.183
Exopthalmo-meter Rt (mm)	-.795	1.122	-.159	-.709	.482
Exopthalmo-meter Lt (mm)	-1.385	1.178	-.279	-1.175	.245
TSH (MU/l)	6.688	3.270	.364	2.045	.046*
FT3 (ng/dl)	-.329	.551	-.138	-.596	.554
FT4 (ng/dl)	.132	.229	.113	.576	.567

It shows that TSH levels are independent predictor of vitamin D Levels in the studied subjects (P<0.01).

CONCLUSION

Our study showed that there is lower vitamin D levels in subjects of group 1 (Graves' disease with exophthalmos) than group 2 and 3. The degree of exophthalmos was inversely correlated with the degree of vitamin D deficiency. There was negative correlation between vitamin D status and free T3 and free T4, and a positive correlation with TSH level but did not reach a statistical significant.

RECOMMENDATIONS

There is prevalence of vitamin D deficiency in Grave s' disease with and without exophthalmos and there is correlation between vitamin D status and thyroid functions and the degree of exophthalmos, so vitamin D supplementation may play an important role in improving thyroid functions and improving the outcome of Grave s' disease and Grave s' ophthalmopathy.

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